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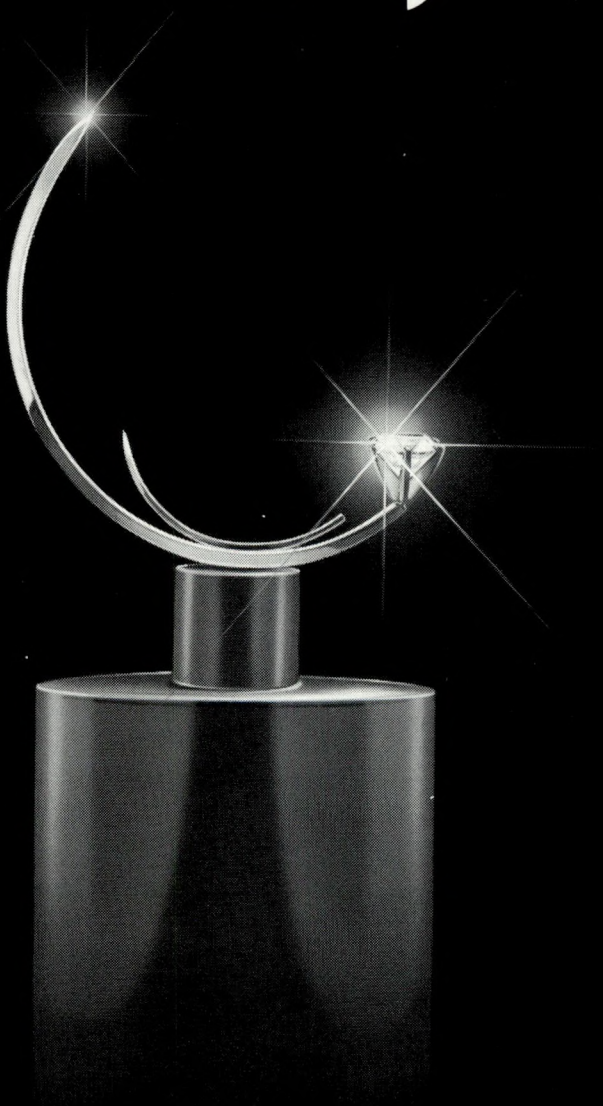

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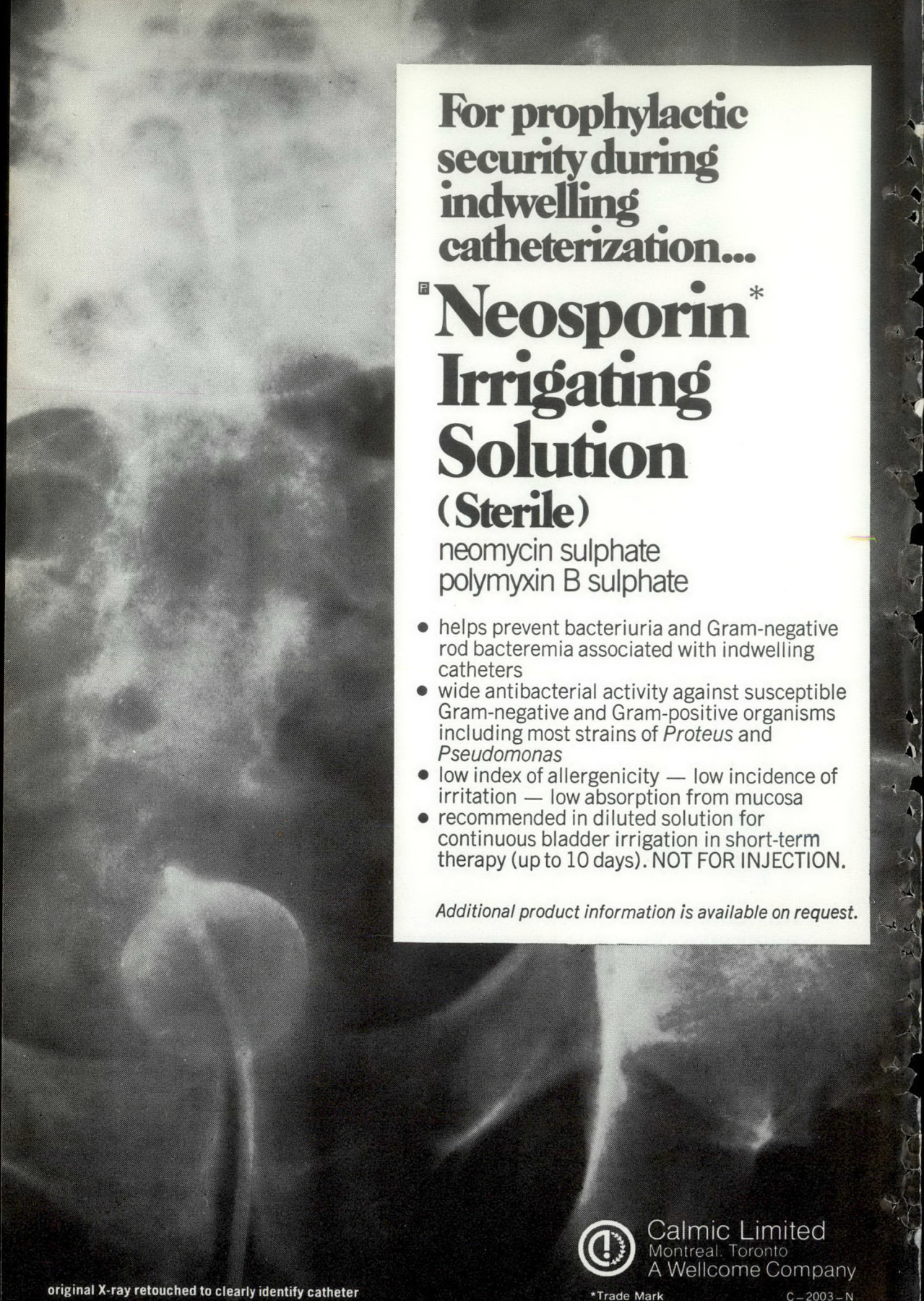

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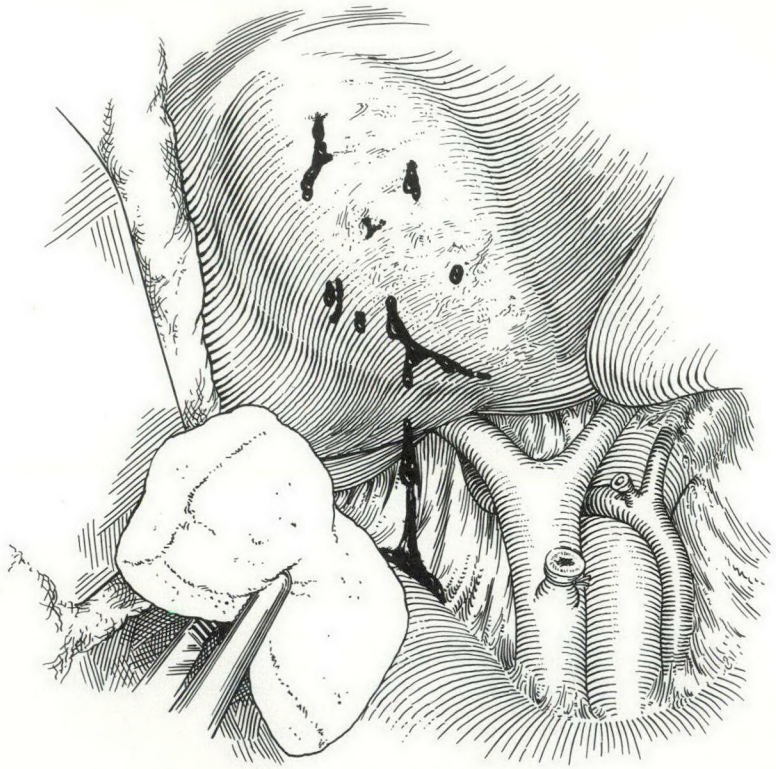

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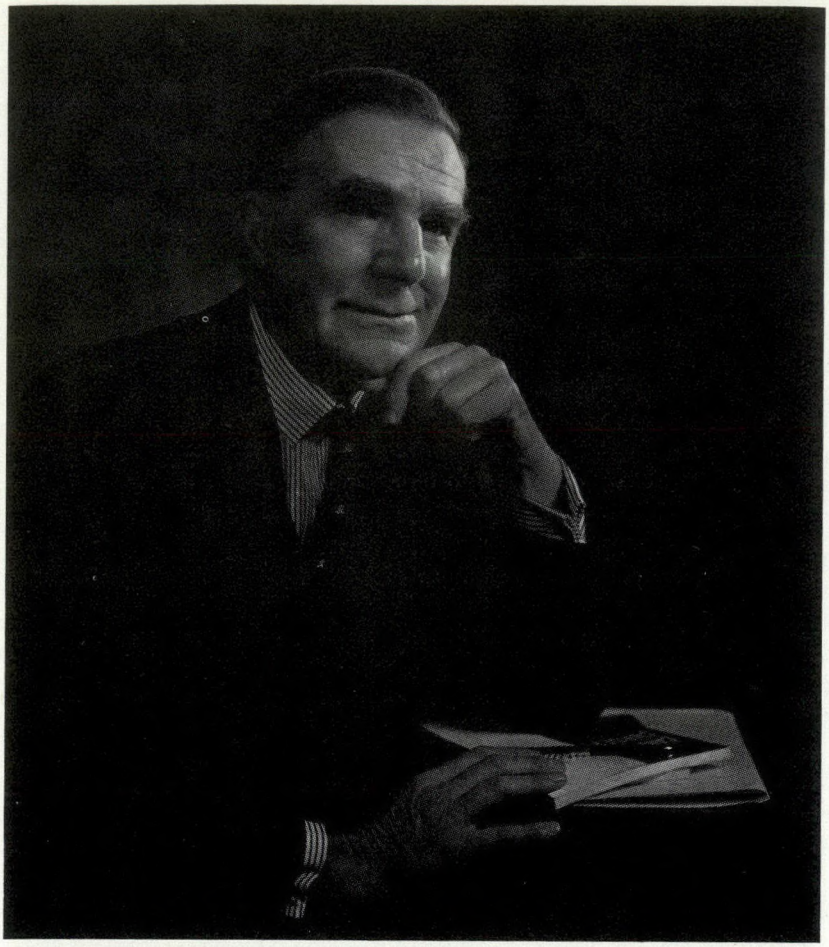

FREDERICK GORDON KERGIN

1907-1974

Dr. Frederick Gordon Kergin died in Toronto on Dec. 20, 1974, at the age of 67. The son of Dr. W. T. Kergin, he was born at Port Simpson in British Columbia in January 1907 and enjoyed an active and highly successful career, becoming one of Canada's most respected and distinguished doctors. During his life he contributed significantly to medical education, the encouragement of surgical research, and the progress of clinical surgery in Canada. All those who knew Dr. Kergin will remember him as an exceedingly bright and perceptive man, a man of unswerving integrity, who had an exceptional devotion to the pursuit of honesty and truth. These qualities were complemented by an intense vitality and a sincere enthusiasm for life, both outside and within the bounds of his chosen profession of medicine.

Dr. Kergin was an outstanding student and achieved many academic honours throughout his life. After elementary schooling in British Columbia, he attended the University of Toronto and graduated with high honours from biology and medical sciences in 1927, and from medicine in 1930. In 1931 he was awarded a Rhodes scholarship and

spent the next 2 years at Oxford University, obtaining a master's degree in physiology and anatomy, again with first class honours. In 1933 he began a 4-year period of postgraduate training in clinical surgery at the University of Toronto (Gallie course) and in London, England. He became a fellow of the Royal College of Surgeons of England in 1935, and of the Royal College of Physicians and Surgeons of Canada in 1939. He was appointed to the surgical staff of the Toronto General Hospital and the teaching staff of the University of Toronto in 1937.

His academic career in surgery was interrupted by World War II, during which he served with distinction in the Royal Canadian Army Medical Corps. He was one of the medical officers who arrived in England in advance of the first Canadian troops in 1941, and he rose to the rank of lieutenant colonel. After the war he resumed his teaching appointment in the department of surgery at Toronto. He became head of the ward "B" service at Toronto General Hospital, and senior surgical consultant at the Toronto Hospital for Tuberculosis. This was during the era when the surgical treatment of pulmonary tuberculosis was at its peak.

In 1957, he was appointed professor and head of the university department of surgery at the University of Toronto, and surgeon-in-chief at the Toronto General Hospital. During his next 9 years of leadership as chairman of the department, research activity was strongly supported and considerably expanded. Dr. Kergin devoted much attention to the further development of postgraduate surgical training at the University and was responsible for introducing the concept of interhospital coordinating committees in the various surgical specialties.

In 1966, Dr. Kergin was appointed associate dean in the faculty of medicine at the University of Toronto. In this capacity, he was actively involved in planning changes in the medical undergraduate curriculum, and he played a major role in the development and conversion of Sunnybrook Hospital to a full-time teaching institution. Beginning in 1971, Dr. Kergin served as a member of the board of trustees at Sunnybrook Medical Centre.

Throughout his career, Dr. Kergin's great vitality and capacity for work involved him with many activities and in many organizations. Thoracic surgery was a special interest from the earliest days, and he achieved distinction as one of the pioneers in this field in Canada, the United States and Great Britain. Amongst the honours accorded Dr. Kergin as a thoracic surgeon were the presidency of the American Association for Thoracic Surgery in 1966, and a Hunterian professorship in the Royal College of Surgeons of England. In postgraduate education he was active in the affairs of the Canadian Royal College and Canadian Medical Association; he was chairman of the editorial board of the *Canadian Journal of Surgery* for many years and a trustee of the R. S. McLaughlin Foundation.

Dr. Kergin was held in the highest regard by his colleagues and students, to whom his personal interest and assistance were a constant stimulus. He is particularly and fondly remembered by his many residents, who will continue to meet annually as members of the Kergin Surgical Society. I was fortunate to be one such resident, and, like many others, will remember Dr. Kergin as a man of outstanding ability and as a friend whose efforts profoundly affected our careers in surgery. With his wife, Suzanne, and their son, Michael, his many colleagues share both sorrow at his death and pride at a life of great accomplishment.

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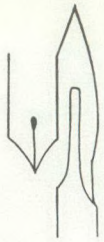

QUILL ON SCALPEL This section provides a medium through which Canadian surgeons can declare themselves, briefly and informally, on the day-to-day affairs of surgery.

THE INTERNATIONAL SYSTEM OF MEASUREMENT (SI) AND MEDICINE

By 1980 Canadians will be accustomed to thinking in terms of measurement units such as kilograms, centimetres and litres rather than the customary pounds, inches and gallons. Physicians are to some extent familiar with the metric system because drugs have long been measured in metric units and the results of biomedical research are usually expressed in the same manner. But fewer physicians and even fewer Canadians in general are conversant with the essence of the current basis of the metric system: Le Système International d'Unités, or the International System (SI) of Units.

SI is a comprehensive specification for units of measurement that is rational and coherent, universal in application and interpretation, and applicable to all scientific disciplines, including medicine. It is the outcome of scientists' efforts to improve the metric system, which, over the years, has left room for error and misunderstanding because of differences in usage in different countries and different disciplines. Many countries now favour SI as a system of measurement; and, in medicine, the logic of SI has convinced physicians in Australia and Great Britain, for example, to change over to SI. But physicians in Canada and the United States have not yet seriously considered SI, even though it offers many advantages for medicine—and even though the introduction of SI into North America seems inevitable. What are SI units and what are their advantages?

SI units are of two kinds, "base units" and "derived units", which are related in a logical mathematic manner. Base units are reference units for specific quantities. There are seven base units: the metre is the base unit for length; the kilogram the base unit for mass; the second, for time; the mole, for amount of substance; the kelvin, for thermodynamic temperature; the ampere, for electric current; and the candela, for luminous intensity. Each unit has a specific definition; for example, the mole is the amount of substance of a system that contains as many elementary entities as there are atoms in 0.0072 kg of carbon-12. Derived units are formed by combining base units according to algebraic relations linking the corresponding quantities. Thus the expression for the newton (the force that gives to a mass of 1 kg an acceleration of 1 $m/s \cdot s$, better written as 1 $m \cdot kg \cdot s^{-2}$) links the base units for mass, length and time. Some derived units are related to other derived units; for example, the pascal (or newton per square metre) is derived from the newton. But the pascal is itself derived from three base units so that, complex as these interrelationships may seem, they are always rational and coherent.

Coherence is a definite advantage of SI because, in the derivation of units from others (essentially from base units) through multiplication and division, unity is the fundamental numerical factor. Calculation is simplified. Calculations are made either in terms of unity or of the power of 10 so that the numerals themselves do not change; only the magnitude of the power of 10 changes. And the decimal basis of the system permits one to limit the range of numerical values in statements to that between 0.1 and 1000. This process is facilitated by the use of specific multiples and prefixes. The length of 0.006 52 m is better written 6.52 mm; and a platelet count of 425 000/mm^3 is just as readily written 425 x $10^3/mm^3$. (In fact, because the litre is the preferred unit for volume, the latter expression should be translated into the expression 425 x $10^9/l$.)

The logic of SI and the facility with which

SI can be used and interpreted in all scientific disciplines in all countries are important advantages of this new system. Scientifically, these two advantages, which stem from coherence and rationality that characterize SI, are attractive but, even so, the objection may be raised that this has little to do with bedside medicine. And besides, opponents ask, have we not been asked to master enough systems of measurement in medicine? Is not our business bedside care?

To answer these criticisms one should consider the advantage of using a unit such as the mole. Its use permits one to determine, and compare, the concentrations of a variety of biochemical substances because a uniform unit system can be applied to measurement of these substances. Preferably, millimoles per litre should be used for most substances. It is thereby possible to consider the biologic relationships of substances as different as glucose, urea, bilirubin, bicarbonate and potassium—and such relationships are less readily appreciated when concentration is based on mass rather than amount of substance. The mole makes biochemical determinations easy to understand in terms of body concentration because the mole is a logical unit for consideration of the concentration of substances in body fluids. Thus the concentration of hydrogen ion is more meaningful in terms of nanomoles per litre than in the dimensionless terms of pH; and the concentration of a polyvalent ion such as phosphate, for which the degree of dissociation and therefore the effective equivalent weight is dependent on pH, is better expressed in molar terms than in terms of equivalents or millequivalents, which make for ambiguities. Osmolal significance of plasma components, too, is better understood in molar terms; one can determine the osmolal significance of these components as well as the osmolality of a fluid of known composition when direct measurement of osmolality is not feasible.

In brief, SI appears to be appropriate for the majority of measurements that physicians deal with. Measurement of some substances, however, still has not been finalized. As one example, hemoglobin cannot yet be considered in molar terms because there is no agreement on the reference species for hemoglobin, and therefore its molecular weight; as another example, it is unlikely that enzyme activity will be considered in molar terms until there is agreement as to method on a molecular basis. But for the commonly determined substances — blood glucose, blood urea nitrogen, serum electrolytes, serum creatinine—interpretation in terms of millimoles per litre is likely to be favoured.

How far one should go is a matter for debate. It appears that the Australians have adopted SI lock, stock and barrel; that is, every measurement is now being reported in SI units whether the measurement is, for example, that of a relatively straightforward analysis such as blood glucose (mmol/l) or even hydrogen ion (nmol/l) or analyses reported in less familiar terms such as acid phosphatase (μmol/min·l), oxygen tension (kilopascals) and vitamin B_{12} (pmol/l). Whether Canadian physicians should accept SI *en bloc* is uncertain but it is important that the matter be debated.

Change for change's sake is unacceptable but SI *is* a logical system of measurement and merits discussion. And there *are* objections to SI. One is related to unfamiliarity. Behind unfamiliarity lurks the spectre of danger to patient care; some physicians believe that any new system will introduce dangers through errors in interpretation. Another objection is the view that SI is one more system of measurement being thrust on physicians by nonmedical scientists; first it was milligrams per cent, then milliequivalents per litre, and now it is to be millimoles per litre. And the notations required by SI are different from those that are familiar to physicians.

Another objection is the lack of suitability of some units for medical purposes. For example, the pascal is to be the unit for pressure; but for blood pressure is not even the kilopascal too large (1 kPa = 7.5006 mm Hg)?

A more serious objection, perhaps, concerns logistics. Apparatus will have to be recalibrated, new report forms will have to be designed, and all health professionals will require re-education. Cost is considered a major factor, and also human change. Change in a human system is always a major undertaking, especially when benefits are difficult to see or are likely to become

evident only after many years. With SI, education of an entire generation may be necessary before benefits become apparent—and there is no doubt that education is the single most important factor determining success of any transition to SI. As yet few medical students are taught SI units but the place of teaching of SI units in medical curricula is a matter of major importance.

Whether the objections to SI are entirely valid for Canadian physicians can be decided only after much debate. It is important that all groups within the Canadian medical profession consider both the objections to and the advantages of SI. It is important because Canadians cannot afford to ignore a system of measurement that many physicians in other countries have wished to incorporate into medical practice. The experience of these other countries and a growing volume of literature is now available for Canadian physicians to study, and it seems appropriate at a time when Canada is introducing the metric system in all spheres that Canadian physicians should examine a specialized aspect of the metric system that is singularly applicable to medicine.

D. A. E. SHEPHARD, MB, FRCP[C]

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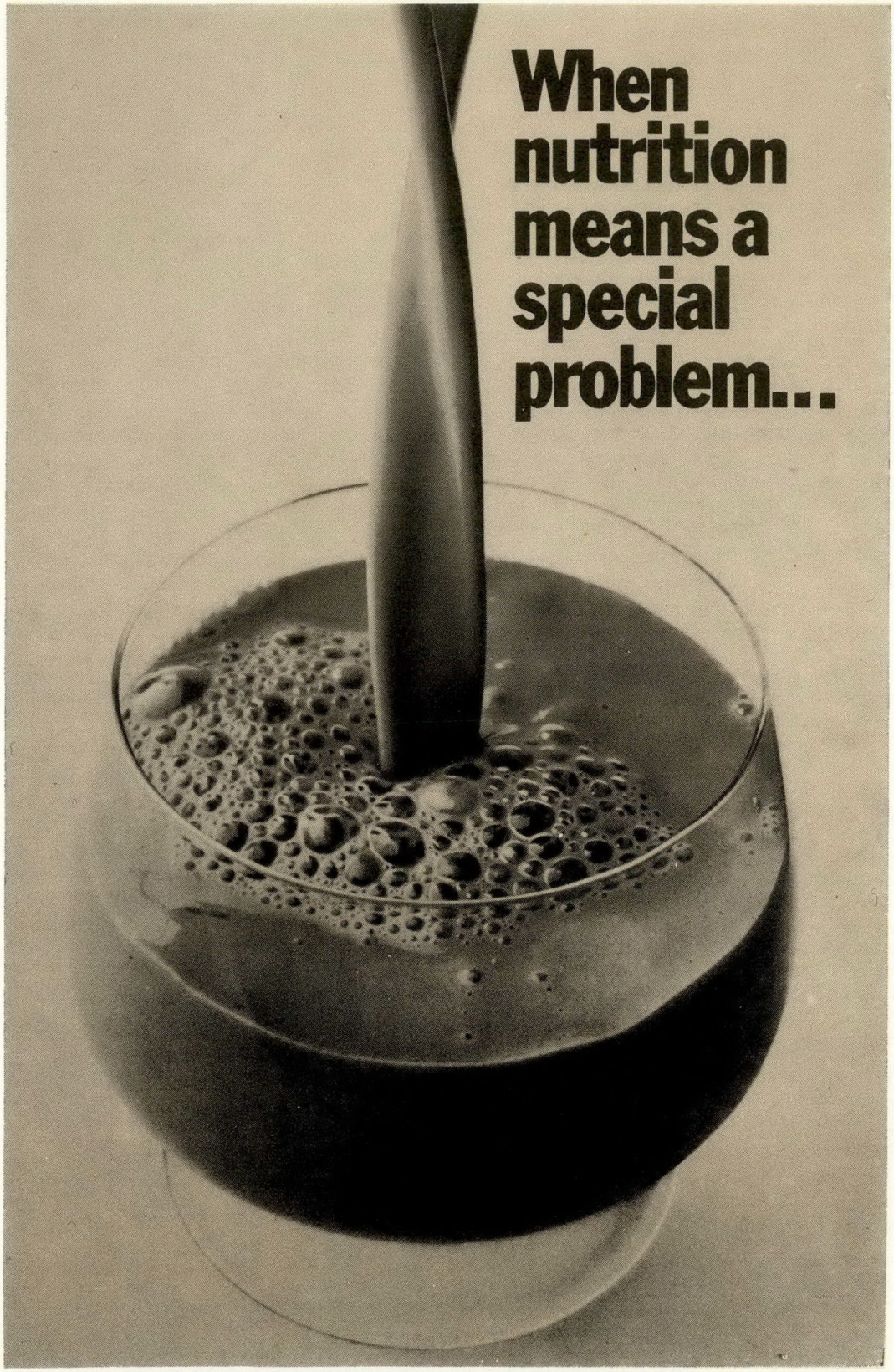
When
nutrition
means a
special
problem...

REVIEW ARTICLE

SOME ASPECTS OF WOUND HEALING RESEARCH: A REVIEW

C. HEUGHAN, MB, BChir, FRCS(Eng), FRCS[C]* and THOMAS K. HUNT, MD†

Summary: Mammalian response to injury essentially is that of tissue repair and re-epithelialization. The most important component of repair tissue is collagen, and after injury collagen turnover is greatly increased. Collagen biosynthesis is initiated by nuclear DNA of fibroblasts; the steps in biosynthesis are complex but studies of collagen biosynthesis may eventually have clinical potential. Normally, wound healing lasts for up to 2 years but nutritional and metabolic factors, such as malnutrition, delay healing; hyperalimentation would likely be beneficial under these conditions. Other factors that influence wound healing are the oxygen tension in tissues, the hemodynamic status, and the effects of substances such as cortisone, vitamins A and C, and zinc.

Résumé: Les mammifères combattent essentiellement les lésions par une réparation des tissus et par une nouvelle épithélisation. Le composant le plus important de la réparation tissulaire est le collagène dont l'activité est considérablement augmentée après une lésion. La biosynthèse du collagène est déclenchée par le DNA nucléaire des fibroblastes. Les étapes de cette biosynthèse sont complexes, mais leur étude peut, en fin de compte, se révéler bénéfique sur le plan clinique. La cicatrisation normale de plaies peut prendre jusqu'à 2 ans, mais certains facteurs, tant nutritifs que métaboliques (la dénutrition notamment), retardent la guérison. Il est probable qu'une suralimentation puisse, dans ces conditions, avoir un rôle favorable. Parmi les autres facteurs qui influencent la guérison des plaies, figurent la tension d'oxygène tissulaire, l'état de l'hémodynamique et les effets de certaines substances, comme la cortisone, les vitamines A et C et le zinc.

WITH increasing specialization among animal species, the capacity to respond to physical injury by regeneration of tissue that has been destroyed has been progressively lost. Mammals are able to regenerate only epithelium, liver and bone. Consequently, mammalian response to injury essentially consists of connective tissue repair and re-epithelialization.

The most important structural component of repair tissue is the fibrous protein, collagen, which, in conjunction with mucopolysaccharides, fills the gap left by injury. Besides acting as a filling material, the collagenous matrix joins the original tissue edges together with a network of interlacing fibres (Fig. 1), and the collagen-mucopolysaccharide matrix forms a bed over which regenerating and migrating epithelium grows, and through which new vasculature penetrates.

This network of collagen is responsible for the mechanical strength of healing wounds, and there is a close correlation between collagen content and tensile strength during the first 2 to 3 weeks of healing.[1, 2]

Recent studies of wound healing have been dominated by analysis of the biosynthesis and chemistry of collagen. This re-

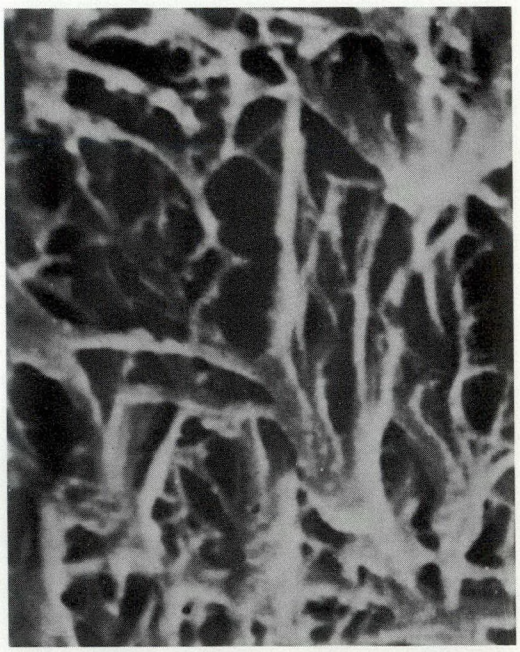

Fig. 1.—Scanning electron microscopic view of wound collagen. Note fine fibres and lack of orientation (x 10 000).

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†Department of surgery, University of California, San Francisco, Calif.

view seeks to correlate recent advances in basic science with findings in the experimental surgical laboratory, and to assess the clinical implications of some recent advances in knowledge of the chemical and nutritional determinants of connective tissue turnover.

Some Aspects of Collagen Biochemistry

Collagen, the chemistry and biology of which have been well reviewed by Grant and Prockop,[3] is a structural protein that is widely distributed throughout the body. It is the major component of tendons and ligaments, it provides a framework on which cells of the parenchymatous organs are mounted, it is responsible for many of the mechanical properties of skin and it provides a pressure casing for the muscular arteries. The basement membrane of cells consists of a unique form of collagen differing chemically from that in other locations in that it contains cysteine.

Physically, collagen is characterized by great tensile strength and lack of elasticity at the molecular level. In the body, however, where it forms a lattice whose interstices are filled with extracellular fluid, collagenous tissue is viscoelastic. Collagen turnover, although normally slow, is greatly increased following injury.

The chief steps of collagen biosynthesis are enumerated as follows:

1. Fibroblast proliferation.
2. Amino acid chain assembly.
3. Hydroxylation.
4. Glycosylation.
5. Extrusion of collagen from fibroblast.
6. Removal of telopeptides.
7. Cross-linking of aldehyde groups.
8. Orientation along lines of stress.
9. Binding to glycosaminoglycans.

During the first 5 days after injury the fibroblast population of the wound increases. Collagen biosynthesis is initiated by the nuclear DNA of the fibroblast, in which each amino acid in the protein is represented by three purine or pyrimidine bases. When collagen production is "switched on", an appropriate chain of base triplets is transferred, in an inverted form, to newly synthesized messenger RNA that travels in the cytoplasm to the ribosome where it dictates the assembly of a chain of amino acids, each link of which corresponds to a particular set of three purine or pyrimidine bases. During this process, some of the proline and lysine residues are chemically modified by the addition of a hydroxyl group, and some of these derivatives are further modified by the addition of a carbohydrate complex to form a glycosylated amino acid.

The hydroxylation of proline is of particular interest. Hydroxyproline is found almost exclusively in collagen; furthermore, it is readily identified by a relatively simple colour reaction, which serves as a method of identification and quantitation of collagen. The conversion of labelled proline to labelled hydroxyproline provides a measure of the rate of collagen synthesis, and the specific activity of the label in hydroxyproline may be used to follow the breakdown of collagen. Proline hydroxylation is effected by prolyl hydroxylase, which requires ferrous iron, vitamin C, molecular oxygen and alpha-ketoglutarate as cofactors. Lack of any of these substances impairs hydroxylation and probably prevents the egress of collagen from the fibroblast. Collagen can only be synthesized from proline and not from available hydroxyproline.

Newly formed collagen leaves the fibroblast and is rendered insoluble by the removal of small segments from the end of the molecule. A deficiency of the enzyme that effects the removal of these fragments has been described in dermatosparaxis, a disease of cattle.[4, 5] The animals have weak skin that fails to heal after injury. In addition, joint and bone deformities often develop. Microscopically, the skin collagen bundles are disorganized. There is no report of a comparable disease affecting humans.

Recently extruded collagen is soluble in cold, neutral salt solutions. With time this property is lost but the polymer remains soluble in cold, dilute acids. Mature collagen is insoluble in both salt and acid solutions. The proportions of salt-soluble, acid-soluble and insoluble collagen may therefore be used as a guide to the rate of collagen turnover.

The changes in the solubility of collagen are due to chemical polymerization, a process that requires the oxidative deamination of some lysine and hydroxylysine residues

to form aldehyde radicals. The aldehyde groups from adjacent molecules then condense to form stable, intermolecular, chemical cross-links. This process occurs at certain specific sites on the molecule; thus, mature collagen has a recognizable crystalline structure.

Cross-linking can be prevented either by blocking the enzyme systems responsible for oxidative deamination with beta-aminoproprionitrile or by blocking the resulting aldehyde radicals with D-penicillamine so that condensation cannot take place. Both experimental and clinical trials of these compounds have been conducted in attempts to limit the undesirable adhesions that may form, for example, after surgery on tendons or in joints affected by rheumatoid arthritis. Although promising, the use of cross-linking inhibitors is not yet sufficiently safe and reliable to justify clinical application.[6, 7]

It appears that some human disorders including acromegaly, myositis ossificans, some cases of osteogenesis imperfecta and possibly Ehlers-Danlos and Marfans syndromes are associated with inherited defects of collagen cross-linking.[8]

The final stages of healing are characterized by orientation of collagen molecules in the direction of lines of stress and the formation of a stable, compound structure of collagen and mucopolysaccharides. Electron microscopic studies have shown that collagen is bound to a proteoglycan matrix;[9] other studies have shown that this is probably achieved by ionic bonding. The nature of the interaction between collagen and the mucopolysaccharide matrix is still unclear. The mucopolysaccharide matrix may determine the aggregation or the orientation of collagen fibres; alternatively, its role may be mechanical.[10-14]

The structural characteristics of collagen are determined by the physical attributes of the interlocking chain of amino acids constituting the molecule. *In vitro,* if there is any major change in this chain—for example, by substituting a proline analogue for proline—the resulting protein is released into the extracellular space at a decreased rate; *in vivo,* a major change leads to diminished wound strength. This finding provides another possible method whereby undesirable scar formation may be limited.[15-18]

Since the physical characteristics of collagen are largely dictated by its molecular structure, it is hardly surprising that collagen shows little species variation. Therefore, observations on laboratory animals can be extrapolated to man.

Despite its great mechanical strength, collagen may be broken down rapidly. The degradation of collagen is known, under some conditions, to be more rapid than its synthesis, and this is true of wounds of almost any age. The mechanisms of this rapid breakdown are incompletely understood, although there are certain pointers. Skin and colonic mucosa taken by biopsy are both capable of breaking down native soluble collagen that has been converted into a gel by warming to body temperature, and some bacteria also show collagenolytic activity. By contrast, serum from some patients contains a factor capable of inhibiting collagenase.[19]

Another possible mechanism for collagen breakdown is by lysosomal enzymes. These include not only collagenase but also enzymes capable of degrading the mucopolysaccharide matrix in which the collagen fibrils are embedded. It seems possible that under conditions of rapid collagen turnover there is a delicate balance between collagen synthesis on the one hand and the net effect of collagen lysis and anticollagenase on the other.[19] Thus, although the rate of collagen turnover is normally slow, in wound tissue it is rapid, and interference with production in the face of an unchanged breakdown may result in disruption of old wounds. The best known example of this phenomenon is scurvy.

Sutures are required to hold before any new collagen is formed. Therefore, until new collagen has been formed, the integrity of the wound depends on pre-existing collagen between each suture and the wound edge. Collagen lysis may be observed in the creeping of retention sutures towards the centre of the wound.

Collagen lysis seems to be to some extent a systemic phenomenon that is induced by trauma. A striking example of this process is the propensity of abdominal aortic aneurysms to rupture after diagnostic laparotomy, even though the aneurysm itself has not been manipulated. The walls of human

aortic aneurysms have no demonstrable collagenolytic activity (Stoney R, Hunt TK, unpublished data).

More precise information on the balance between collagen synthesis and collagen lysis will probably elucidate the mechanisms not only of normal healing but also of the overabundant production of connective tissue that produces, for example, keloid scars, and the defective connective tissue production that is exemplified in patients receiving glucocorticoids. Similarly, the etiopathogenesis of diseases characterized by destruction of normal collagen or destruction, or overproduction, of basement-membrane collagen, may eventually be understood, so that their control may be given a rational basis.

Some of the amino acids resulting from the biodegradation of collagen are used in subsequent biosynthesis.[20, 21]

The Sequence of Normal Healing

The tensile strength of incised wounds builds up similarly in all species. Although the general pattern is the same, the time scale varies. Fig. 2 shows the pattern of this build-up, which can be conveniently divided into three overlapping stages.

During stage 1, the wound edges are only tacked together with fibrin. The classic changes of acute inflammation are taking place together with debridement, by macrophages, of dead tissue, foreign particles and bacteria. Fibroblasts are proliferating.

During stage 2, which lasts from about the 5th to the 15th day, rapid collagen synthesis is reflected by a rapid rate of gain in tensile strength.

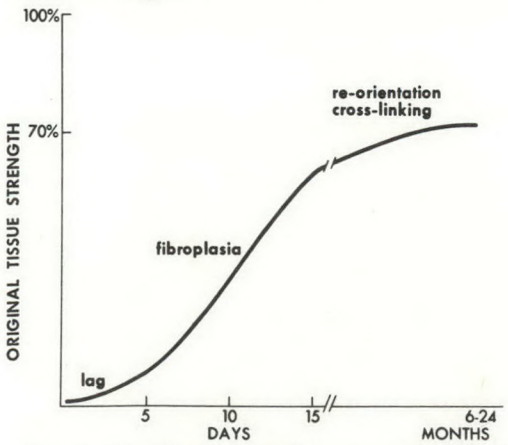

Fig. 2.—Tensile strength-time curve for incised wounds.

Stage 3, which lasts between 6 months and 2 years, is characterized by a slow increase in tensile strength that is attributable to orientation of the collagen fibres in the direction of strain, to cross-linking and to the formation of a stable collagen-mucopolysaccharide matrix.

Nutritional and Metabolic Factors in Repair

The assembly of the amino acid chains during the primary stage of collagen biosynthesis is normally a rapid process. It is theoretically possible that starvation and protein deficiency may interfere with the formation of collagen; however, newly synthesized wound collagen is derived partly from the amino acids that appear through local collagen breakdown.[20] Thus, severe and prolonged negative protein balance is likely to impede repair, and, under such conditions, hyperalimentation would likely be beneficial. Although mild hypoproteinemia should not delay healing, the resulting edema does inhibit collagen synthesis.

Under normal circumstances, proline hydroxylation is the rate-limiting step of wound collagen synthesis. Experimentally, healing may be delayed by a lack of any of the cofactors for prolyl hydroxylase. Thus, both hypoxia and scurvy cause defective collagen synthesis.

Under conditions of adequate nutrition, which normally exist in western countries, the rate-limiting factor in collagen biosynthesis is the rate of delivery of oxygen to the repair cells. The observation by Cousteau and his team of divers that their wounds healed more rapidly when they had been breathing an oxygen-rich atmosphere (Po_2, about 300 mm Hg) has stimulated experimental and clinical work on the effects of breathing oxygen on wound healing.[22-25]

During active collagen synthesis, the oxygen tension (Po_2) in the wound space of experimental wounds is only 10 mm Hg. An increase in the oxygen concentration of the inspired air, although promptly increasing the Pao_2, leads to a delayed and comparatively small response in the extracellular oxygen tension in the wound, and faster collagen synthesis. It has been postulated that the low extracellular Po_2 in wound tissue is attributable to both limitation of the diffusion of oxygen from the capillary to the

fibroblast and to a high demand for oxygen by the repair cells. This view was corroborated by the observation that wounds in experimental animals heal more rapidly in terms of collagen synthesis, gain in tensile strength and increase in DNA content when the animal breathes oxygen at concentrations up to 70%. Above this concentration, healing is impaired because of the separate problem of pulmonary oxygen toxicity. Breathing a mixture containing only 12% oxygen leads to a gain in both tensile strength and collagen accumulation, per unit time, that is slower than normal.

Administration of 40% oxygen should accelerate the rate of healing of primary human wounds by about 15%, and in extensive wounds with dead space this increase may approach 50%. It appears that, at least in theory, administration of an oxygen-rich gas mixture should be useful, both clinically and economically, in treating extensive wounds.

The delay in healing rate that occurs as the result of a diminution in oxygen availability is of practical importance. In hypovolemia there is a decrease in wound Po_2, and restoration of the circulating volume with blood or with dextran leads to restoration of the normal Po_2 and collagen synthesis rate.[26]

Wound Po_2 is also decreased in hypervolemia induced by an intravenous injection of normal saline (dose, 2.5 to 10 ml/kg).[27] It seems likely that the decrease in Po_2 results from local edema increasing the intercapillary distance. A corollary of this observation is that any other cause of edema, such as hypoproteinemia, is also likely to delay healing resulting from an increase in the distance across which oxygen must diffuse from capillary to collagen-forming cell. It seems possible that tissues other than granulation tissue—for example, brain and kidney—may be similarly affected by generalized edema.

Anemia has been incriminated as a cause of defective healing, despite the fact that the normal physiologic mechanisms are able to counteract its effects to some extent.[28-31] Several groups of workers have been unable to demonstrate any impairment of wound Po_2 or a collagen synthesis due to mild, uncomplicated, normovolemic anemia.[32, 33] Clearly, gross anemia will affect oxygen delivery; it seems likely that the effect is only significant when the hematocrit is 20% or less.

Major, remote trauma has several hemodynamic effects.[34] These include hemodilution, anemia and hyperviscosity due to an abnormally high concentration of circulating macromolecules, particularly fibrinogen. Experimentally, the intravenous injection of high-molecular-weight dextran, which mimics the circulatory disturbances that normally follow major trauma, decreases both wound tissue Po_2 and collagen synthesis per unit time; "clinical" dextran produces a similar but smaller effect.[35]

Gas tensions at various points in the advancing granulation tissue may be measured directly by use of a microelectrode introduced into the wound tissue; in rabbits this fills a plastic chamber implanted into the ears. The result of such recordings is shown diagrammatically in Fig. 3.[25, 36, 37] The Po_2 close to a wound capillary is between 60 and 80 mm Hg. Near the advancing edge of granulation tissue, approximately 100 μm away, the Po_2 approaches zero. In this zone of very low oxygen tension, the main cells are macrophages, which are capable of engulfing bacteria (even in such a hypoxic environment) but not of killing them.[38] A major component of intracellular killing of bacteria is oxygen-dependent.[39]

Nearer to the capillary there is a zone where the oxygen tension gradient is ex-

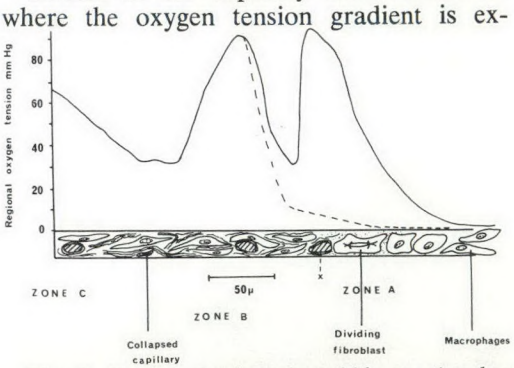

Fig. 3.—Oxygen tensions in rabbit ear-chamber granuloma. Left side represents oldest part of wound containing mature collagen; right side is advancing edge of healing tissue adjacent to central space. (Reproduced by permission from SILVER IA: Local and systemic factors which affect proliferation of fibroblasts, in *Biology of Fibroblast. Proceedings of Sigrid Juselius Symposium, Turku, Finland, August 1972*, edited by KULONEN E, PIKKALAINEN J, New York, Academic Press, 1973.)

tremely steep and it is in this region that actively proliferating fibroblasts, together with a few fibres of recently formed collagen, may be found. Behind the capillary, the fibroblast population is more sparse and fibres of presumably cross-linked collagen are more abundant.

Oxygen tension in the centre of an experimental granuloma may be measured by means of other techniques. Fluid may be sampled from the central dead space filling an implanted stainless-steel, wire-mesh cylinder and then injected into a standard gas analysis apparatus.[23] This method may be modified by filling the cylinder with Teflon tubing perfused with anoxic saline. Since Teflon is permeable to oxygen, the Po_2 of the central dead space equilibrates with that of the saline perfusing the tube, which can then be measured continuously with a standard Clark type of electrode (Fig. 4).[40]

A further refinement consists of burying a Silastic tube (length, 10 cm) in a subcutaneous tunnel. The tube is perfused with anoxic saline whose oxygen tension equilibrates with that in the surrounding wounded tissue.[41] The Po_2 of the saline is then measured with standard apparatus. Because the tissue reaction around an implanted tube is minimal, the gas tension measured is a closer approximation to "normal" tissue than in other techniques. This method has been tried in man,[42] and may be of value in monitoring Po_2 in patients who have either respiratory or circulatory disturbances likely to impair tissue oxygenation. It can also be used to measure Pco_2 (Fig. 4).

These methods measure the Po_2 in the centre of the wound, the net result of supply from the capillaries and demand by the healing tissue. A decrease in Po_2 implies a decrease in delivery of oxygen which may

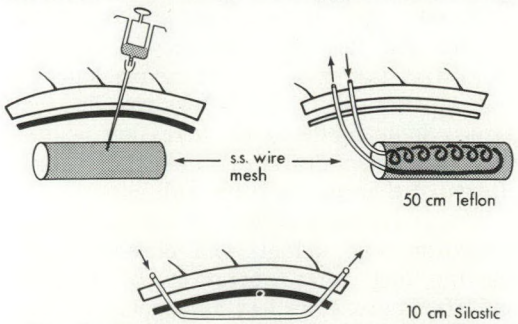

Fig. 4.—Indirect methods of measuring Po_2 at centre of wound.

be due to increased viscosity, to plasma changes or to changes in Pao_2. Experimentally, it is possible to confirm that oxygen delivery has been impaired by weighing the collagen that has accumulated in an experimental wound over a given period.

Cortisone and Healing

One action of glucocorticoids, in common with other anti-inflammatory drugs, is stabilization of the lysosomal membrane. This decreases the activity of lysosomal enzymes released into the wound during the first stage of healing and thus diminishes the local amino acid pool available for subsequent repair. Experimentally, glucocorticoids only impair healing if given in suppressive doses during the first 5 days after wounding.

The effect of cortisone on the lysosomal membrane is directly antagonized by vitamin A, which is a lysosomal labilizer. Experimentally, cortisone-retarded healing can be restored towards normal by the local or systemic administration of vitamin A.[20, 21] There are now some 50 clinical cases in which healing of wounds of patients who were being treated with glucocorticoids was induced with either topical or systemic vitamin A (Hunt TK, unpublished data). Vitamin A appears to restore fibroplasia and epithelialization, but not wound contraction, towards normal.

Zinc and Healing

In a number of clinical reports it has been suggested that healing is impaired by zinc deficiency, and in others attempts have been made to show that heavy losses of zinc from burn surfaces may lead rapidly to deficiency in a previously normal patient. However, we believe that the case for routine supplemental zinc is as yet not proved.

Experimental work shows that zinc has a fundamental role in protein synthesis in unicellular organisms as well as in amino acid utilization in the rat liver; the zinc-deficient rat also is less able to incorporate labelled glycine and proline into collagen. In addition, zinc deficiency may impair cross-linking.[43-50]

Infection and Healing

Comparatively little is known about the effect of infection on healing.

The majority of pathogenic bacteria consume oxygen so that the Po_2 of infected wounds is normally low or zero.[51] A decreased amount of collagen in experimental granulomas infected with *Proteus sp.*, has been reported. The reason for this is not clear. It may be either the "steal" by bacteria of all the available oxygen or a high rate of collagen breakdown possibly due to the presence of bacterial or granulocyte collagenase. The effect of infection on cross-linking is unknown.[52]

In animals rendered completely devoid of circulating granulocytes by the administration of antileukocyte serum, healing can occur normally.[53]

Although macrophages are able to engulf bacteria in an environment with a Po_2 of only approximately 1 mm Hg, intracellular killing is poor. During the intracellular killing of bacteria and fungi, the rate of oxygen consumption by phagocytes increases. This increased oxygen demand reflects a change to aerobic metabolism of glucose by the hexose monophosphate shunt, and is not shown by the leukocytes of some patients with deficient phagocytic microbicidal function and an accompanying susceptibility to infection. Energy for phagocytosis can be derived from the anaerobic glycolytic pathway.[38]

There is a correlation between the severity of infection in experimental granulomas of rabbits and the concentration of environmental oxygen. The bacterial count in wound fluid is lowest in animals breathing 40% oxygen and highest in those breathing 12% oxygen.[54]

After extensive burns, there is a derangement of serum immunoglobulin patterns resulting in a decreased efficiency of the defence mechanisms against infections.[55, 56] It seems possible that stimulation of the phagocytes, possibly with oxygen, may be a valuable adjunct in the prevention of sepsis after thermal injury.

Clinically, hyperbaric oxygen therapy in osteomyelitis is reportedly of value.[57]

Healing in Some Special Sites

Colon

The mechanical strength of normal colon is provided almost entirely by the submucosal collagen.

The colonic epithelium has a high collagenase activity, which increases proximodistally. Hence, colonic anastomoses in rabbits have virtually no bursting strength for the first 3 to 5 days. Furthermore, because of collagen lysis, the bowel may rupture anywhere within 2 cm on either side of an anastomosis. This finding suggests one reason why low anterior resections have such a high rate of leakage.

Inoculation of the peritoneal cavity with pathogenic bacteria has no effect on the build-up of bursting strength, but the addition of foreign materials (e.g. sterilized feces) to the region around the contaminated anastomosis caused a prolonged delay in the restoration of normal bursting strength.[58]

It appears therefore that, although bacterial contamination itself has little effect on colonic healing, the additional presence of feces or other foreign material, including blood or plasma, is likely to delay healing; as a result, the anastomosis may require protection with a proximal colostomy or cecostomy.

Arterial Intima

Injury to the intima of an experimental animal in the presence of a high concentration of serum lipids produces a fatty lesion, analogous to human atherosclerosis.

In these lesions, which are avascular, the Po_2 may decrease to between 5 to 12 mm Hg. This may partly explain the inability of the arterial wall to remove unwanted fats.[59] There is little evidence of new collagen formation in these early fatty lesions. The chemical profile of the fat in the arterial wall shows changes that may reflect the changing Po_2 profile.

Other Sites

Despite the increase in knowledge of healing and its allied science of collagen chemistry, little is known of the mechanisms and kinetics of collagen turnover in scar tissue. Some methods of increasing healing rate have been described and some of the effects of therapy have been discussed.

The converse problems of excessive scar formation (e.g. keloid) and of undesirable scarring (e.g. after operations on tendons and after burns) are less amenable to manipulation. The use of cross-linking inhibitors

or of proline analogues is a promising possibility.

Abnormalities of collagen metabolism occur in a wide variety of diseases. Apart from the abnormalities in atherosclerosis, the abnormality in peptic ulceration may be regarded as a defect in healing and that in hepatic cirrhosis as an example of repair occurring in an organ that normally heals by regeneration.

A greater understanding of the mechanisms of collagen breakdown and of the immunology of collagen can hardly fail to add perspective to the study of such diseases as rheumatoid arthritis and diseases involving the destruction of basement membranes. Some transplantation antigens may be associated with the collagen molecule.

These possible lines of research potentially are of clinical usefulness from the delineation of the antigenically active sites on the human collagen molecule.[60] This raises the theoretical possibility of inhibiting collagen-anticollagen reactions by the use of synthetic blocking antibodies.

Conclusions

In this review only a few aspects of a vast subject have been discussed. Such vital and rapidly advancing subjects as wound contraction, and the migration and regeneration of damaged epithelium have not been considered.

Establishment of a relationship between clinical practice and research is a highly desirable end product of basic surgical research and a justification of the expenditure of public money. A 15% increase in the rate of healing gained by breathing 40% oxygen at atmospheric pressure, the possibility of restoring cortisone retarded healing towards normal with vitamin A and the demonstration that transfusion of patients with mild postoperative anemia in order to assure normal healing is unnecessary, facilitate such a relationship. The discovery of other factors influencing wound healing is both likely and imminent.

Every period of major progress in surgery has been achieved by a productive union with one of the basic sciences. Future advances may originate in a fruitful (if polygamous) union with biochemistry and immunology.

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INTERPRETING THE RATE OF SURVIVAL IN CARCINOMA*

CHANDLER SMITH, MD†

Summary: Carcinomas originate in one organ, spread away from that site, cannot be accurately staged, and require total ablation for cure. Cure is achieved when all of the tumour is located within the tissue ablated by the method used. The rate of survival indicates the proportion of patients with such localized disease. A comparison of survival rates is not a comparison of therapeutic accomplishments; it is a comparison of the cumulative localization of the tumours in different series. The superior method is that which ablates the primary tumour and the largest amount of surrounding expendable tissue at the earliest time. Selecting the method according to this principle rather than by a comparison of survival rates provides the highest prospect for cure. That is the purpose of treatment.

Résumé: Les cancers prennent naissance dans un organe, se propagent ailleurs à partir de cet organe. Leurs étapes successives ne peuvent être déterminées avec précision. Pour guérir, ces tumeurs doivent être excisées complètement. La guérison n'est obtenue qu'à la condition que la totalité de la tumeur soit localisée dans l'organe excisé par l'acte chirurgical pratiqué à ce moment. Le taux de survie indique la proportion de malades souffrant de cette tumeur localisée. Une comparaison des taux de survie, comme telle, ne reflète pas les résultats thérapeutiques et ne permet pas de comparer ces derniers. Ce n'est que la comparaison de la localisation cumulative des tumeurs dans des séries différentes. La méthode par excellence est celle qui consiste le plus tôt possible à exciser, et la tumeur primaire, et la quantité maximum des tissus avoisinants susceptibles d'être le siège de métastases. Seule une méthode conforme à ce principe et non pas celle qui consiste à comparer des taux de survie, permet de formuler le meilleur pronostic de guérison. C'est le but même du traitement.

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In evaluating cancer therapy, it is customary to equate the rate of survival with the quality of the method so that a comparison of survival rates will reveal the superior method of treatment. The premise of this practice is that random classification by clinical staging will establish parity of tumour spread in the groups of patients to be compared. This method of analysis is presently used in studies of carcinoma of the breast, colon, endometrium, uterine cervix, and other organs.

Staging, Tumour Spread and Survival

That clinical staging establishes parity of tumour spread is in doubt. Haagensen and Stout,[1] for example, reported that among 253 patients with carcinoma of the breast in whom the axillas were clinically normal, 49% were subsequently found to have metastatic tumour in their axillary lymph nodes. Shah, Rosen and Robbins[2] reported a similar experience. Others have observed that different examiners assign different stages of the disease to the same patient, and "positive axillas" were detected in one-third of patients who did not have breast cancer.[3] In view of this, comments on the "fallacy" of the practice of clinical staging[4] are not surprising. The same point could be made about staging of carcinomas of organs other than the breast; the clinical estimate of metastatic disease in the mesenteric lymph nodes for cancer of the colon, or in the pelvic lymph nodes for carcinoma of the endometrium or uterine cervix, is scarcely more accurate.[5-9]

Although clinical staging may be grossly inaccurate, it is nevertheless true that spread of the tumour dominates the rate of survival. Consider a carcinoma in a single patient. If the tumour is localized within the tissue ablated by the method, cure is assured; if the tumour is spread beyond the tissue ablated by the method, failure is certain. The spread of the tumour, therefore, determines whether the patient will survive or succumb. If the spread of the tumour determines the survival of the individual, it also determines the survival of the group.

Thus, the rate of survival is dominated by the cumulative spread of the tumours at the time treatment is applied. In an actual sense this conception is also borne out; metastatic disease in regional lymph nodes regularly portends an unfavourable result for cancers of the breast, colon, uterus, and other organs.

If tumour spread cannot be accurately assessed before treatment, and if tumour spread dominates the rate of survival, it is apparent that the rate of survival cannot be a reliable index of the quality of the method. One may therefore ask, "What does the rate of survival express?" It is obvious, on the one hand, that without treatment there will be no rate of survival, and, on the other, that the result of treatment will be affected by the unpredictable spread of the tumours. The interpretation of survival rates should therefore be expanded to accommodate both factors. Accordingly, the rate of survival indicates the proportion of patients in which the tumour was localized within the tissue ablated by the method of treatment—or, more simply, the proportion of patients with localized disease. The rate of survival is never an absolute figure, but its reliability increases with the passage of time.

This interpretation widens the meaning of the rate of survival so that it accommodates both the amount of tumour tissue ablated, which is the contribution of the method, and the extent of the tumour spread, which is unpredictable before treatment is given. The latter prevents one from equating the rate of survival with the quality of the method alone. Thus, the pronounced effect of tumour spread on the result of treatment cannot be denied, yet the incorporation of this effect into the meaning of the rate of survival precludes its traditional use as an index of therapeutic achievement.

The proper interpretation of survival rates may be illustrated in two examples. A high survival rate does not indicate a superior method so much as the localization of the tumours within the tissue ablated by that method in many of those patients. Conversely, a low survival rate does not fault the method so much as indicate a deep spread of the tumours beyond the tissue ablated by that method in many of those patients. Thus, a comparison of survival rates is not a comparison of the quality of the two methods of treatment; it is a comparison of the cumulative data concerning localization of the tumours in two series of patients.

Identification of the Superior Method of Treatment

If the rate of survival does not express the quality of the method, how is the superior method to be identified? It is to be identified from considering the biologic features of the tumour. It is evident that the tumour arises in one organ, and that later it may spread from that site; the extent of spread is not accurately discernible from clinical examination of the patient, and cure requires the ablation of all of the implanted tumour. These features forecast the principle of treatment: the ablation of the primary tumour and the largest amount of contiguous expendable tissue at the earliest possible time. What is "expendable" depends on the site of the tumour and the condition of the patient, so an arbitrary judgment about expendability is unavoidable. Nevertheless, the boundaries of that judgment can be foreseen; that is, the method cannot be so radical as to jeopardize the patient's recovery, and it cannot be so conservative as to allow recurrence from residual tumour left in expendable tissue. Between these limits, which must be judged individually for each patient, lies the highest prospect for cure.

The method that complies with this principle of treatment is radical therapy. The superiority of the radical method, however, is reflected only in the occasional patient in whom the tumour has spread to the regional lymph nodes but not beyond. Otherwise, in cases of carcinoma of the breast, for example, the radical and conservative methods succeed equally because the tumour is localized to the site of origin, or fail equally because the tumour has spread beyond the regional nodes. In these instances both methods achieve the same result. Nevertheless, the patient who can be cured only by the radical method cannot be identified before treatment is given, therefore, the highest prospect of cure for

all patients is ensured only when the method is selected according to principle of treatment rather than by a comparison of survival rates.

For cancers of the breast and uterus, the principle of treatment favours the radical method because the axilla in the former instance and the adnexas in the latter are expendable tissues that may be sacrificed without an increase of mortality over conservative methods. Radical treatment for carcinoma of the colon, however, may not be superior because the mortality of abdominoperineal resection is likely to be a more critical factor than the gain derived from the extra tissue ablated by that method, as Crile and Turnbull have pointed out.[10] In this instance, the radical method may violate the principle of treatment by excessively jeopardizing the recovery of the patient. The implacable question the surgeon cannot avoid is whether the higher prospect for cure by the radical method justifies the increased mortality of that procedure. Only the surgeon, who is aware of his own skill, the condition of his own patient and the relative risk of the conservative and radical methods, may answer this question.

Realistic Interpretation of Survival Rates

As long as the tumour spreads only away from the site of origin, and cure requires the ablation of all of the tumour, the result of treatment cannot be improved by reducing the amount of tissue ablated by the method or by delaying the application of it. This claim is not invalidated by poor survival rates after radical treatment or good results after conservative therapy. For example, good survival after conservative treatment allows the possibility that a radical method used in its place might have achieved an even better rate of survival. On the other hand, a poor result after radical treatment disallows the possibility that conservative therapy applied to those same patients could have improved that result. Regardless of the rate of survival, therefore, compliance of the method with the principle of treatment provides a result that cannot be improved by any method that does less. Accordingly, the superior method is not that which occasionally achieves a high rate of survival; it is that which consistently complies with the principle of treatment.

The comparison of survival rates is also affected by a realistic interpretation of them. Because the rate of survival expresses the proportion of patients with localized cancer, it is evident that the result after conservative therapy might be improved by a method that does more, but the result after radical treatment cannot be improved by a method that does less. A comparison of survival rates provides no way to conclude that the conservative method is superior or that the radical method is inferior, and massive undertakings for this purpose have no way of succeeding.

The proper interpretation of the rate of survival also allows expression of the biologic nature of the tumours. Highly aggressive tumours tend to be deeply spread and associated with poor results, whereas indolent tumours tend to be sharply localized and associated with good results. The proposed interpretation thus accommodates the "biologic predeterminism" of MacDonald.[11]

The recommended interpretation, does not include a consideration of vascular, hormonal, or other factors that determine the extent of the tumour spread. Nor should it. Although, these factors may be important in determining the particular extent of the tumour at the time of treatment, it is only the fact of that spread that determines whether the individual, or the series of individuals, will survive. Such considerations are therefore neither unimportant nor germane to the interaction between tumour distribution and tissue ablation.

A method of treatment is said to "achieve" a certain rate of survival. This implies that the method is the sole cause of the result. The suggested interpretation of survival rates, however, disputes this because it incorporates the biologic nature of the tumours. In order to emphasize this biologic effect, and to dampen the implication that the method is the sole cause of the result, it would perhaps be useful to relabel the rate of survival as the "tumour localization index" or some similar term. This would emphasize the observation that the biologic nature of the cancers *vis-à-vis*

the method, rather than the method alone, determines the result of treatment. Moreover, it is closer to the truth than a term that calls no attention to this biologic effect. A more realistic term would also encourage consideration of the tumour-host relationship. This is altogether appropriate as immune factors come to have an increasingly prominent role in oncology.

Finally, there is no statistical way of verifying the proposed interpretation of survival rates. Just as it is an intellectual exercise to presume that the rate of survival is determined by a single factor—the method of treatment—so is it an intellectual exercise to realize that the results of treatment are determined by two independent factors—the extent of the tumour spread and the tissue ablated by the method. What stands to the credit of the dual factors is the registered inaccuracy of clinical staging and the established observation that metastatic disease at the time of treatment decidedly affects the rate of survival. Those who contend that the rate of survival expresses the quality of the method alone must either proclaim the precision of the clinical staging or deny that tumour spread dominates the result of treatment.

One concludes that the rate of survival is determined by two factors, each independent of the other, that the rate of survival unreliably expresses the quality of treatment, and that a comparison of survival rates cannot be expected to identify the superior therapy for several common primary cancers. The principle of treatment is sound, and compliance with this principle rather than making a comparison of survival rates is the surest guide to the best therapy. This combination of a realistic interpretation of survival rates and a sound principle of tumour therapy defeats the old, enduring difficulties; that is, it allows the superior method to be identified, it guarantees the highest prospect of cure for all patients and it permits survival rates to be understood usefully in terms of the tumour-host relationship rather than erroneously in terms of the quality of the method of treatment. These are the benefits of a realistic interpretation of survival rates.

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FRACTURES OF THE MEDIAL HUMERAL EPICONDYLE IN CHILDREN*

W. B. BEDE, MD, A. R. LEFEBVRE, MD and M. A. ROSMAN, MD, FRCS[C]

Summary: A review of 50 children with fractures of the medial humeral epicondyle facilitated a simple classification of this injury and its management. The "apparent isolated" fracture of the medial humeral epicondyle is uncommon; it is more frequently associated with elbow dislocation, with or without spontaneous reduction, at the time of injury. Analysis of the results of treatment of medial humeral epicondylar fractures in this group of children showed that, in the case of those with an "apparent isolated" injury, treatment with a sling only gave good results in 90% whereas poorer results followed open treatment or fractures associated with dislocation. Closed treatment is therefore recommended. Open reduction is indicated only with (a) ulnar neuritis at the time of injury or (b) intra-articular fragment.

Résumé: Une revue de 50 cas de fractures de l'épicondyle huméral interne chez l'enfant a facilité une classification simple de cette lésion et de son traitement. La fracture "apparemment isolée" de l'épicondyle huméral interne est une rareté clinique. Elle est plus souvent accompagnée de luxation du coude, avec ou sans réduction spontanée, au moment de la lésion. L'analyse de nos résultats thérapeutiques dans ce groupe d'enfants a révélé que, dans le cas de lésion "apparemment isolée", le traitement consistant dans le port d'une simple écharpe a donné de bons résultats dans 90% des cas, tandis que nous n'avions que des résultats médiocres après réduction ouverte ou dans les cas de fractures accompagnées de luxation. Nous conseillons donc le traitement fermé. La réduction ouverte n'est indiquée que si l'on note (a) une névrite cubitale au moment de la blessure ou (b) la présence d'un fragment intra-articulaire.

FRACTURE of the medial humeral epicondyle and its association with total dislocation of the elbow was first described in 1851 by Cooper. A classification of this injury was proposed by Watson-Jones,[1] who noted an incidence of 25% of associated elbow dislocations. Since then, Smith[2] has accumulated the largest published series of medial epicondylar fractures; he has concluded that conservative treatment gives the best results, even with gross displacements, except when the fragment is intra-articular or there is ulnar neuritis.

In this paper we review the results of treatment of 50 cases of fractures of the medial humeral epicondyle in childhood. This total comprises 22 "apparent isolated" fractures of the medial epicondyle (Fig. 1) and 28 epicondylar fractures associated with known dislocation of the elbow (Fig. 2). These fractures were seen at the Montreal Children's Hospital from Jan. 1, 1960 to May 1, 1974. We present evidence to support the idea that this apparent isolated injury is often associated with a dislocation of the elbow that reduces spontaneously, and that, if not seen on the original radiographs of the injury, is evident at follow-up clinical and radiologic examination. We propose a classification of this injury that will help physicians in its management.

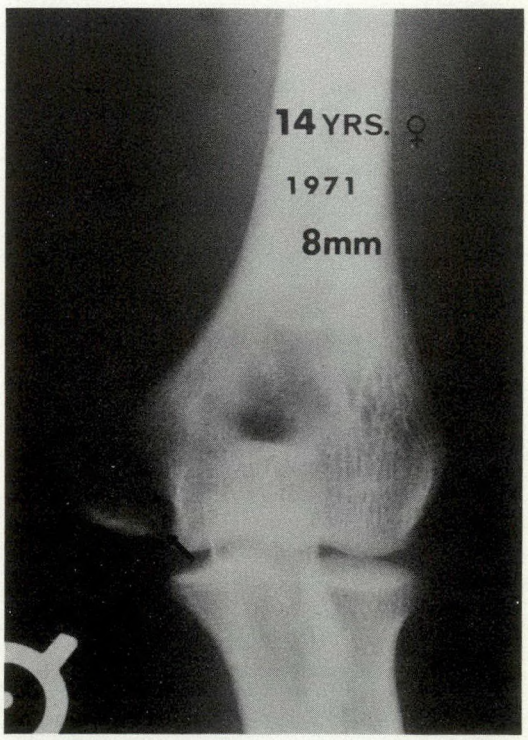

Fig. 1.—Isolated fracture of medial humeral epicondyle.

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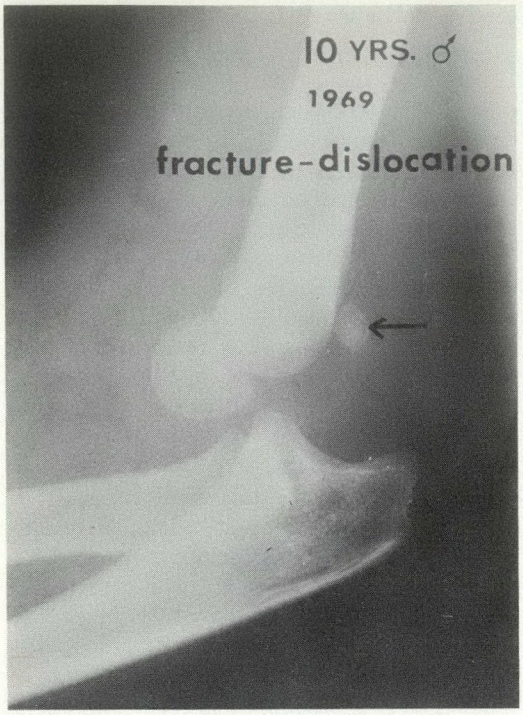

Fig. 2.—Fracture of medial humeral epicondyle with known dislocation of elbow.

Findings of Study

Details of Patients

During the period 1960 to 1974, 50 patients were seen with fractures of the medial humeral epicondyle. The mean age at injury was 12.5 years (range, 6.0 to 17.9 years), closely paralleling the appearance and fusion of the apophysis of the medial epicondyle. The mean follow-up period was 3.7 years.

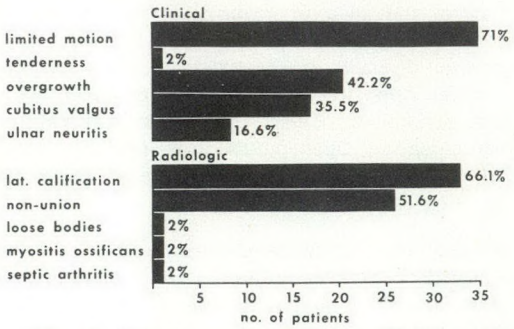

Fig. 3.—Summary of total complications for all patients (both fracture groups considered together).

TABLE I.—Mean Displacement of Apparent Isolated Fractures and Fractures Associated with Dislocation

	Nos. of patients and displacement (mm)					
Fracture group	*1-3*	*4-6*	*7-10*	*11-15*	*Intra-articular*	*Total no. of patients*
Apparent isolated.....	7	2	13	0	0	22
Associated with dislocation.....	3	0	7	1	17	28

TABLE II.—Results of Treatment of 50 Patients with Apparent Isolated Fractures and Fractures Associated with Dislocation

		Result(%)*	
Fracture group	*Treatment*	*Good*	*Poor*
Apparent isolated fractures (n = 22)	Immobilization only (n = 13)	90	10
	Open reduction (n = 9)	75	25
Associated with dislocation (n = 28)	Closed reduction only (n = 21)	72	28
	Closed followed by open reduction (n = 7)	50	50

*For criteria see text.

TABLE III.—Classification of Injury (Related to Stress Force)

	Type of injury	*Displacement*
I	Simple fracture	0 - 4 mm
II	Fracture-dislocation with spontaneous reduction	5 mm and over
III	Fracture-dislocation	At level of joint or intra-articular

Classification of Fractures

There were two groups of fractures: (1) 22 apparent isolated fractures and (2) 28 fractures and associated elbow dislocation. The mean displacement of the fracture in the two groups is shown in Table I. Displacement was 10 mm or less in patients with isolated fractures, whereas in the majority of patients with associated dislocation the displacement was intra-articular.

Methods of Treatment

Of the isolated fractures, 13 were treated by immobilization and 9 by open reduction (Table II). The mean displacement in the former was 4 mm and in the latter 9 mm. Treatment of fracture with dislocation was by closed reduction of the dislocation (21 cases), or by closed reduction of the dislocation followed by open reduction of the fracture (7 cases). The mean displacement in the first group was 4 mm and in the second group, 8.5 mm.

Immobilization time was about equal whether the fracture occurred in isolation or was associated with dislocation; the average was 34.7 days and 32.1 days respectively.

Results of Treatment

The overall results were assessed by clinical and radiologic examination at follow-up. The result was judged to be good when, subjectively, the elbow was functional, painless and stable and was not grossly deformed and, objectively, range of motion was less than or equal to 15% of normal, cubitus valgus was less than 10°, there was no tenderness, and no clinical ulnar neuritis. Results that did not meet these criteria were considered poor, or unacceptable. Table II summarizes the findings at follow-up. With apparent isolated injury, immobilization alone gave good results in 90% of cases, whereas open reduction gave good results in only 75%, taking into consideration all degrees of displacement. With fractures associated with dislocation of the elbow, closed reduction alone gave good results in 72%

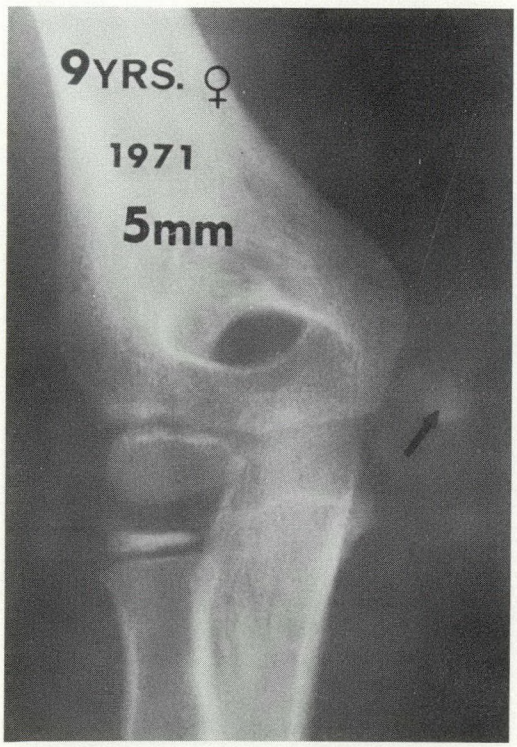

Fig. 4a

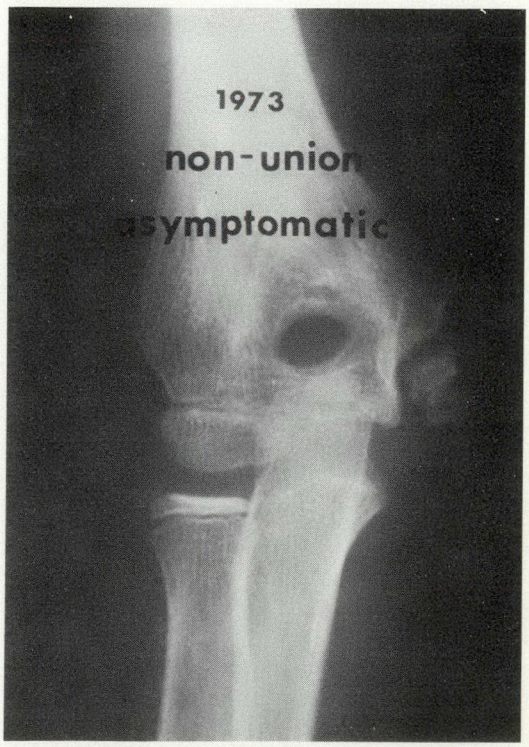

Fig. 4b

Fig. 4.—Nonunion complicating apparent isolated fracture. (a) Fracture with 5-mm displacement in 9-year-old girl treated in plaster splint only. (b) Asymptomatic nonunion 2 years later with good result.

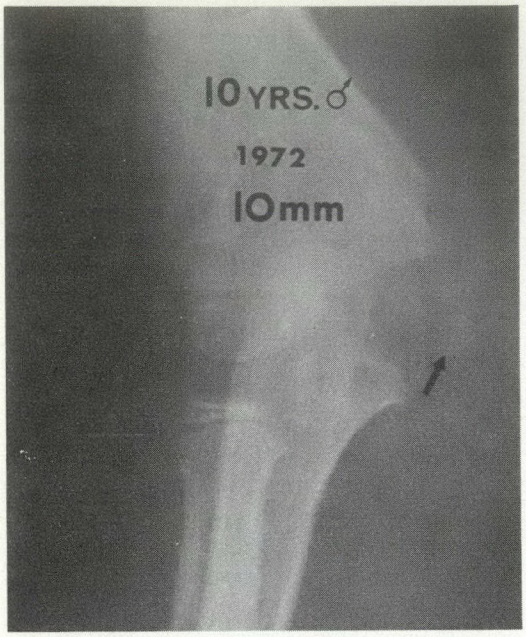

Fig. 5a

Fig. 5b

Fig. 5.—Nonunion and clinical valgus deformity and valgus instability complicating apparent isolated fracture. (a) Fracture with 10-mm displacement in 10-year-old boy treated by open reduction. (b) Nonunion with deformity and instability 1 year later with poor result.

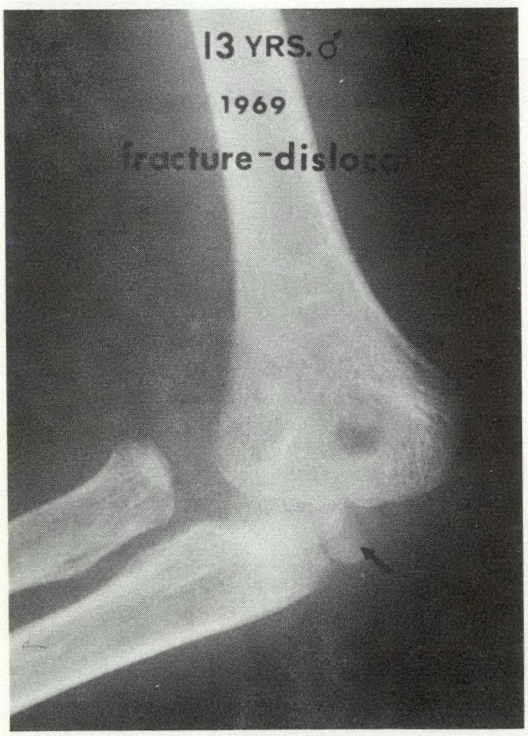

Fig. 6a

Fig. 6b

Fig. 6.—Nonunion complicating fracture associated with dislocation that was not intra-articular. (a) Fracture with 4-mm displacement after closed reduction of dislocation and application of plaster splint only. (b) Asymptomatic nonunion 4 years later, good result.

of cases and closed reduction followed by open reduction gave good results in only 50%.

Complications

Complications were divided into clinical and radiologic for both groups together (Fig. 3). Nonunion with associated complications is illustrated in Figs. 4 to 7.

Discussion

In fractures of the medial humeral epicondyle with associated dislocation of the elbow, the periosteum is separated from the humeral metaphysis at the time of dislocation. Calcification may occur in this area during the healing period leaving long-lasting radiologic evidence of the dislocation (Fig. 8). Lateral periosteal calcification was seen in 55% of medial epicondylar fractures with associated dislocation and in 11% of apparent isolated fractures in this series. This supports the assumption that a proportion of the children presenting with apparent isolated fractures actually sustained a dislocation of the elbow with a spontaneous reduction at the time of injury.

Results were more unsatisfactory and complications were more frequent in patients who presented with associated dislocation than in children with isolated fractures and also in those treated by open rather than closed reduction of the fracture. Closed reduction is therefore advocated for all patients, except those presenting with either signs and symptoms of ulnar neuritis or in an intra-articular medial epicondylar fragment. Mobilization of the elbow is recommended as soon as the acute symptoms of the injury resolve.

Table III provides a simple classification for this injury: (1) simple fracture, without dislocation; (2) fracture associated with a dislocation, with spontaneous reduction; (3) fracture and dislocation without spontaneous reduction. Correlation of this classification to management only occurs with type 3 injury with an intra-articular fragment, which requires open reduction.

Conclusions

A review of 50 cases of medial humeral epicondylar fracture, with or without associated dislocation of the elbow, allows us

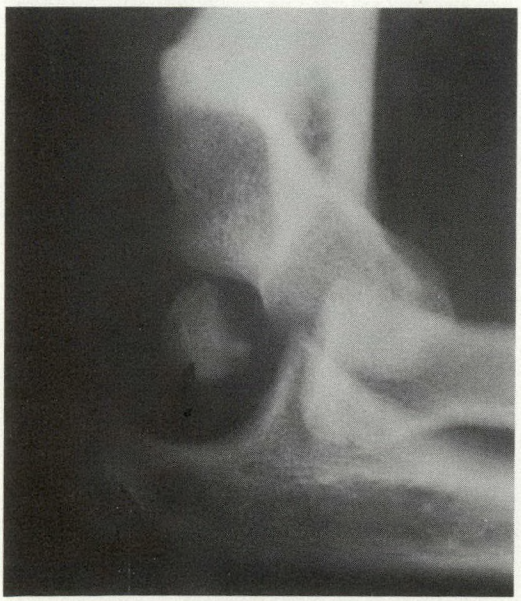

Fig. 7a

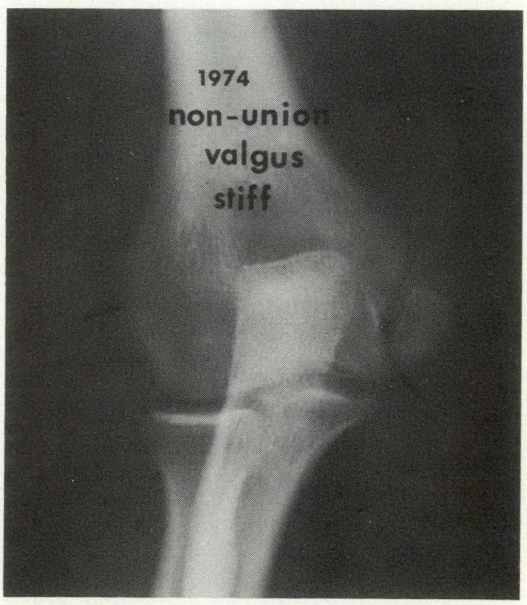

Fig. 7b

Fig. 7.—Nonunion, valgus deformity and stiffness of elbow complicating fracture-dislocation of elbow with intra-articular medial epicondylar fragment in 13-year-old girl. (a) Treatment by closed reduction of dislocation produced extra-articular medial epicondyle, displaced 4 mm; this was splinted only. (b) Tender nonunion with deformity and stiffness of elbow 4 years later with poor result; note lateral calcification.

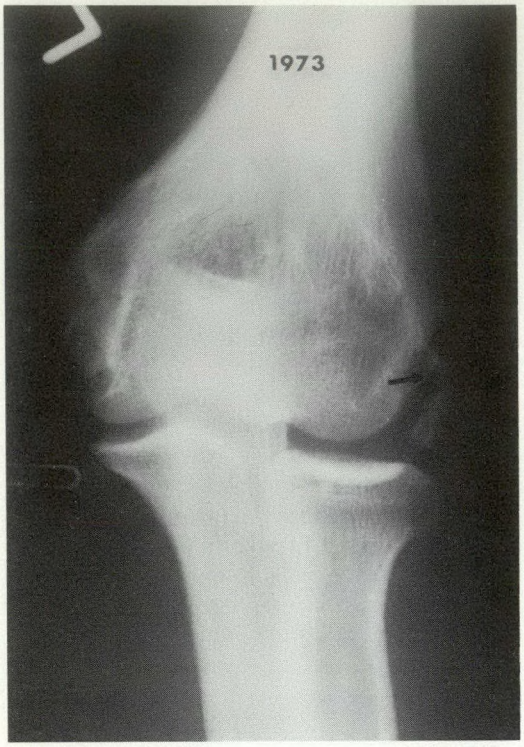

Fig. 8.—Long-term follow-up radiograph of fracture associated with dislocation of elbow showing lateral periosteal calcification.

to conclude that there are only two indications for open reduction with medial epicondylar humeral fracture of the elbow:

1. signs and symptoms of ulnar neuritis, and
2. the presence of an intra-articular fragment that remains intra-articular after closed reduction of the elbow dislocation.

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EFFECTS AND PREVENTION OF FROSTBITE IN WOUND HEALING

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Summary: Observations on wounds sustained at subfreezing temperatures in husky dogs and in man suggested that exposed wet tissues readily become frozen. Frostbite of wounds caused tissue necrosis, wound sepsis and delayed healing, but immediate wound suture protected against this sequence. To explore the effect of wound closure on healing of frostbitten tissue, healing of paired dorsal wounds was studied in 20 rats. In each animal one wound was sutured and the other was left open. In 10 animals both wounds were frozen with Dry Ice. All sutured wounds healed primarily. Most of the control open wounds had healed at 15 days, but in the frozen wounds healing was delayed and infection ensued.

It is suggested that at temperatures much below freezing the immediate treatment of a wound should include prevention of frostbite by wound closure.

Résumé: L'observation de plaies subies à des températures inférieures au point de congélation par des chiens esquimaux et par l'homme, permet de croire que des tissus organiques mouillés et exposés au froid gèlent rapidement. La gelure de plaies entraîne la nécrose tissulaire, l'infection des plaies et retarde la cicatrisation, mais la suture immédiate de ces plaies protège le sujet contre cette séquence pathologique. Pour explorer l'effet de la suture des plaies sur la cicatrisation des plaies gelées, nous avons étudié la cicatrisation de plaies dorsales symétriques chez 20 rats. Chez chaque animal, nous avons suturé une plaie et l'autre est demeurée ouverte. Chez 10 de ces animaux, les deux plaies ont été gelées avec de la neige carbonique. Toutes les plaies suturées ont guéri par première intention. La majorité des plaies ouvertes des "témoins" ont guéri en 15 jours, mais concernant les plaies gelées la cicatrisation a été retardée et elles se sont infectées.

Nous croyons donc qu'aux temuératures bien au-dessous du point de congélation, le traitement des plaies doit comporter la prévention des gelures par une suture immédiate.

As a medical officer on an Antarctic expedition some years ago, I noticed that lacerations sustained by husky dogs in fights healed poorly. The wounds became necrotic and infected, with regional lymphadenitis and abscess formation. These dogs were kept out of doors all year and the temperature, which averaged −15°C, at times reached −35°C. I also noted that if the lacerations were sutured immediately, wound infections did not develop. Details of healing of 19 wounds were recorded. The wounds of four dogs were not sutured; all became infected, healing was delayed and antimicrobials were required to effect healing. The 13 wounds treated by primary suture, however, all healed rapidly without infection. The other two wounds were sutured after 3 and 7 days and both healed satisfactorily with slight delay. A further observation was that infections developing in the open wounds were consistently more severe than infections of similar unsutured lacerations sustained in a temperate environment. Open lacerations in husky dogs froze solid at these temperatures, and it appeared that the wet blood and tissue fluids accelerated the freezing process.

A concomitant observation concerned frostbite in a man who sustained a seemingly trivial laceration of a great toe from an unpared adjacent toenail. The blood from the great toe laceration froze, frostbite of the great toe ensued and ultimately the distal part of the great toe was lost.

It seems that the presence of wet blood and tissues is of paramount importance in the development of frostbite in wounds; if this wetness could be prevented then frostbite would be unlikely. It is well known that tissue necrosis, usually accompanied by wound infection and delayed healing, develops once deep frostbite has occurred,[1-4] but there appears to be no information about the influence of wet blood and tissues as factors in the development of frostbite in wounds. This paper reports the results of experiments made to investigate this.

METHOD

After anesthesia had been induced in 20, white, albino, Wistar rats (weight range, 200 to 630 g) with pentobarbital (2 mg/100 g), the hair over the dorsal region was clipped short with electric clippers. Two

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incisions (length, 2 cm) were then made on either side of the dorsal spine, each wound being extended through the latissimus dorsi, trapezius and erector spinae muscles. The wound on the left side was sutured with three or four interrupted silk sutures; the wound on the right side was left open (Fig. 1). In 10 of the rats both dorsal wounds were then frozen solid by direct application of solid carbon dioxide (Dry Ice) for 4 to 10 minutes (the smaller animals would not tolerate more than 6 minutes of local freezing), and in the other 10 (controls) the wounds were not frozen. The skin and underlying tissue became frozen to a depth of about 0.3 cm. The wounds were then allowed to thaw and the animals to recover from the anesthetic in their cages at a room temperature of 22°C. The unhealed area of each wound was measured twice weekly. Wound swabs were taken for culture from all discharging wounds at intervals from the 6th to 19th day. The animals were killed on either the 15th or 19th day. The wounds were then biopsied.

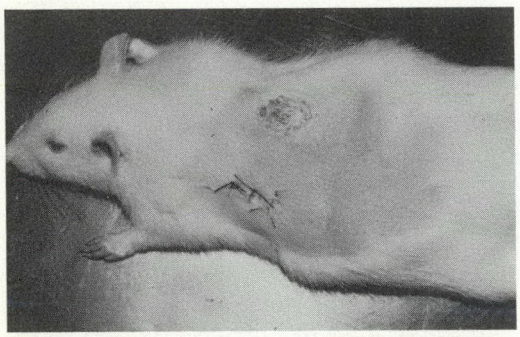

Fig. 1.—Sutured and open wounds. Note frostbite of open wound.

Results

Skin closure was found to protect against deep frostbite injury. There was primary healing of all 10 control, sutured wounds and of 8 wounds that were sutured and then frozen (Fig. 2). Two sutured and then frozen wounds partly broke down on the surface and discharged pus, apparently due to superficial frostbite injury.

In the open wounds, healing was delayed. The area of open wound that was unhealed at 15 days for both frozen and control wounds can be determined by reference to Figs. 3 and 4. With one exception the unsutured wounds in the control rats were almost healed at 15 days. In contrast, the frozen, unsutured wounds were largely unhealed at 15 days and showed the typical microscopic appearance of frostbite with coagulative necrosis and necrotizing myositis (Fig. 5). These results were highly significant when Student's t test was applied ($P < 0.001$).

The duration of freezing also influenced healing. The unsutured wounds that were frozen for 8 to 10 minutes had healed less than those frozen for 4 to 6 minutes (Fig. 6).

Most of the wounds were dry and scabbed and unsuitable for culture. Of the discharging wounds all cultures grew *Staphylococcus aureus,* two grew *Streptococcus fecalis,* one grew *Pseudomonas pyocyaneus,* one grew

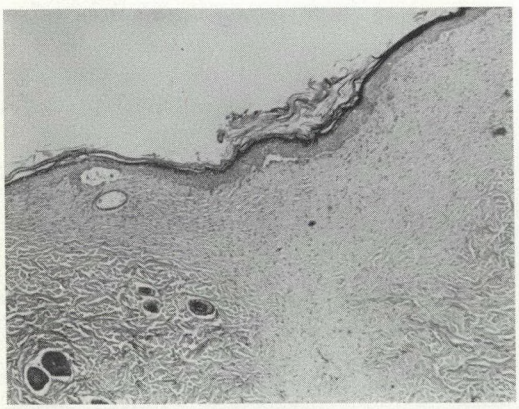

Fig. 2a

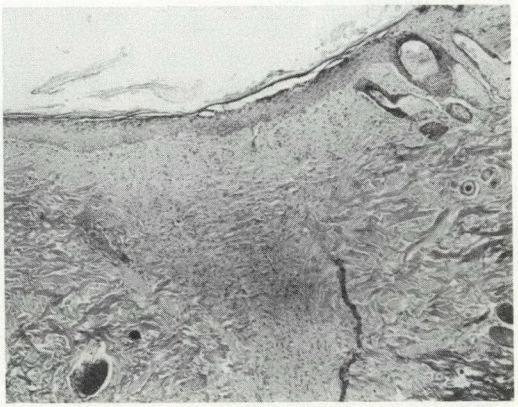

Fig. 2b

Fig. 2.—Healing of sutured wounds. (a) Unfrozen wound (control) (hematoxylin and eosin, x 128). (b) Frozen wound (hematoxylin and eosin, x 128).

Proteus mirabilis and one grew *Enterobacter*. In contrast, only one of the unfrozen control wounds grew a pathogenic organism —alpha hemolytic streptococcus.

Discussion

The histologic changes seen in these experimental frostbite injuries are similar to those demonstrated by Lewis[1] and are similar to those developing after a thermal burn. The progression of change in deep frostbite of an open deep wound to tissue necrosis and frequent severe wound infection, and the protection from this sequence of events afforded by simple wound closure have been demonstrated by the present experiments.

The effect of a low environmental temperature on the rate of wound healing has been investigated in rabbits by Filston and Vennes,[5] who showed that an environmental temperature of −7°C slowed the healing rate of wounds in rabbits' ears. In this study a low environmental temperature during wound healing was not considered pertinent.

During World War II the number of German and Russian military and civilian casualties in eastern Europe was estimated at 20 million.[6] Of these, 3 million must have been sustained at temperatures substantially below freezing, and many of these wounds must have become frozen. Physicians who served on eastern European front noticed freezing of gunshot wounds, especially where the skin wound was extensive. In civilian practice in Canada it is likely that every year a number of accidental wounds occur at freezing temperatures. The application of the results of this study suggest that at temperatures much below zero a wound should be prevented from becoming frozen by immediate first-aid wound closure by taping, clipping or suturing, or by the use of a hot pack applied to the wound. This does not mean that the general principles of surgical management of a contaminated

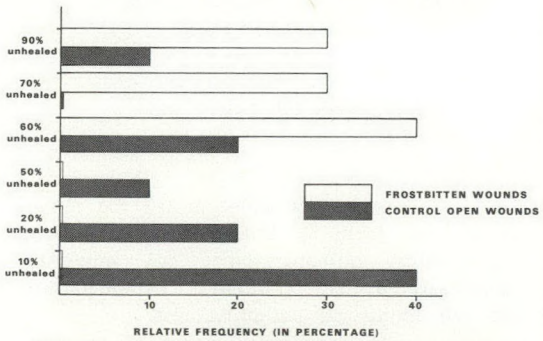

Fig. 3.—Healing of open wounds at 15 days. Note frequency of different areas of unhealed tissue for unfrozen and frozen wounds. Difference between unfrozen and frozen wounds is significant ($P < 0.001$).

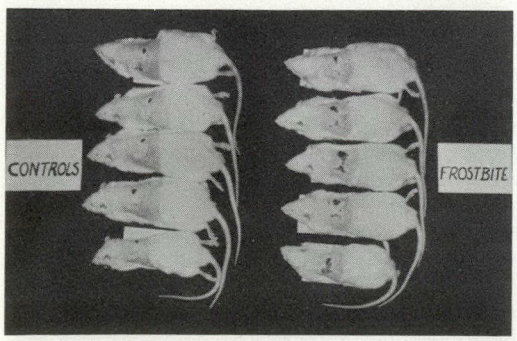

Fig. 4.—Appearance of five typical control animals and five typical wound-frozen animals at 15 days.

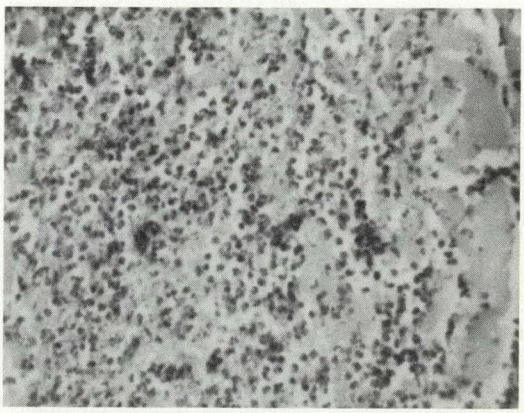

Fig. 5.—Unhealed centre of frozen open wound. Photomicrograph after 15 days; note necrotizing myositis (hematoxylin and eosin, x 320).

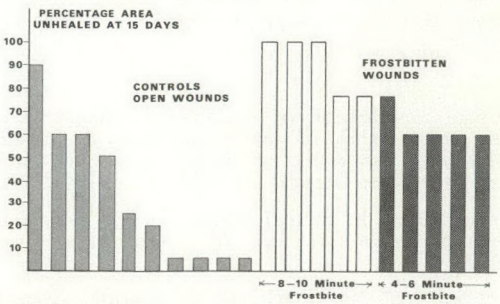

Fig. 6.—Effect on open wound healing of increased exposure to freezing. Each column represents one open wound in one rat.

wound should be neglected. As soon as the casualty has been evacuated to a surgical facility, the wound may still have to be cleansed, debrided and then sutured or packed open, as circumstances dictate.

I wish to thank Major General J. W. B. Barr (ret.), formerly surgeon general, and Dr. R. H. Lowry, director of the Defence and Civil Institute of Environmental Medicine, Downsview, Ont. for encouragement in this project; Drs. R. G. Yaworsky and J. A. Minielly of St. Joseph's Hospital, Hamilton, Ont., for help with the photomicrographs; Dr. J. Biennenstock for facilitating the use of the animal laboratory at McMaster University Medical Centre; and especially Dr. W. S. Myles of the Defence and Civil Institute of Environmental Medicine for many helpful suggestions.

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OSTEOID OSTEOMA AND OSTEOBLASTOMA: RECLASSIFICATION OF 43 CASES USING SCHAJOWICZ'S CLASSIFICATION*

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Summary: Forty-three cases of benign osteoblastic tumour of bone from the University of British Columbia bone tumour registry have been reviewed and reclassified according to the classification of Schajowicz and Lemos. Their classification has the advantage that the relationship of the two lesions is recognized and overlap, both radiologically and microscopically, is allowed for. The terminology used in the new classification, however, is cumbersome and confusing and appears to be of no great advantage. We therefore recommend instead the terminology modified from that of Dias and Frost, which incorporates the observations put forth by Schajowicz and Lemos: (a) cortical osteoblastoma, (b) medullary osteoblastoma, (c) periosteal osteoblastoma and (d) multifocal osteoblastoma.

Résumé: Nous avons passé en revue 43 cas de tumeur osseuse ostéoblastique bénigne enregistrés dans les archives des tumeurs osseuses de Colombie-Britannique et les avons reclassifiés d'après la classification de Schajowicz et Lemos. Cette dernière présente l'avantage d'identifier la relation existant entre les deux lésions et tient compte du chevauchement, tant au point de vue radiologique que sur le plan microscopique. Malheureusement, la terminologie utilisée dans la nouvelle classification est incommode, prête à confusion et, en définitive, ne présente pas de grands avantages. Nous conseillons donc de la remplacer par la terminologie modifiée d'après celle de Dias et Frost qui incorpore les observations mises au point par Schajowicz et Lemos: (a) ostéoblastome cortical, (b) ostéoblastome médullaire, (c) ostéoblastome périostique et (d) ostéoblastome multifocal.

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THE entity known as osteoid osteoma was so named by Jaffe[1] in 1935, on the basis of five cases. Some concern persisted about the distinction of osteoid osteoma from Brodie's abscess and from Garré's sclerosing osteomyelitis, but by 1940 Jaffe and Lichtenstein[2] had reported 35 cases, and the concept of this entity was generally accepted. By 1945 Jaffe[3] had collected reports of 62 cases and had described the appearance of osteoid osteoma in both cortical and cancellous bone. These reports, and that of Sherman,[4] clearly delineated the entity with a distinctive clinical presentation, radiologic appearance and pathologic characteristics.

BACKGROUND

Osteoid osteoma, which generally occurs under the age of 20 years, is more common in males and can involve any bone, though tibia and femur are the most common sites.[5] It is considered to be a benign neoplastic disease of bone[2] with a fairly well-established natural history.[6-8] Certain habitually discussed clinical features—night pain and aspirin relief—remain a mystery but it has been shown to be hypervascular[9] and to contain nerve fibres.[10] Radiologically, it appears characteristically as a central radiolucency with surrounding sclerosis, depending on its origin in cancellous or cortical bone. Grossly, the appearance of a central nidus is characteristically noted as a dark-red spherical or oval focus of cancellous-like bone, surrounded by ivory-like sclerosis. Microscopically, the nidus consists of osteoid trabeculae in a vascular connective-tissue stroma. In adjacent bone, periosteal reaction has been reported,[11, 12] as have changes in adjacent joints.[12, 13] In addition, severe growth disturbance has been reported in association with osteoid osteoma in two cases,[14] and recurrence has been recognized as distinctly possible.[15]

In 1932 Jaffe and Mayer[16] described a tumour of a metacarpal bone containing osteoblastic osteoid tissue and noted certain similarities of this tumour to osteoid osteoma. The lesion seems to have been the same condition described in 1954 as giant osteoid osteoma by Dahlin and Johnson[17] and as osteogenic fibroma of bone by Golding and Sissons.[18] These lesions became accepted as benign osteoblastoma as a result of reports by Jaffe[19] and by Lichtenstein[20] in 1956. The distinction of this condition from osteoid osteoma was based mainly on its larger size and lack of reactive sclerosis. By 1964 Lichtenstein and Sawyer[21] were able to add 20 more cases to their original 11 and to describe it as a benign osteoid-forming and bone-forming tumour occurring particularly in the limb bones, the vertebral column, and the calvarium most often in children or teenagers. Lichtenstein and Sawyer emphasized that the radiographic features are not distinctive, but generally a benign osteoblastoma is lucent and well circumscribed. Sometimes it may appear mottled. If, however, there is much surrounding sclerosis, Lichtenstein and Sawyer prefer to call it osteoid osteoma, even if the lesion is larger than usual.

Microscopically, benign osteoblastoma can be distinguished from osteogenic sarcoma by its lack of nuclear atypism and mitoses; from giant cell tumour by the presence of much more bone and osteoid; and from osteoid osteoma largely on the basis of size and lack of surrounding sclerosis,[21] but also by its more cellular appearance with abundant osteoblasts.[19]

Paralleling the occurrence of the periosteal osteoid osteoma and anticipating Schajowicz's classification,[22] Lichtenstein and Sawyer[21] reported two cases of osteoblastoma of periosteal origin, later referred to also by Goldman.[23]

The similarity of the two lesions implied by the earlier description of Dahlin and Johnson[17] of giant osteoid osteoma is therefore apparent, but most authorities still insist on regarding them as separate entities based primarily on their clinical and radiologic differences. However, we have found that clinically, radiologically and pathologically the increasing number of borderline lesions with features of one or the other entity make dogmatic designation difficult. Accordingly, the attempt by Schajowicz and Lemos[22] in 1970 to place these two lesions, *osteoid osteoma* and *benign osteoblastoma,* in proper perspective and to account for some of these borderline lesions appealed to us. These authors proposed a classification incorporating all the observed features

of both conditions, based on 142 cases of "osteoid osteoma" and 42 of "benign osteoblastoma". Their classification, in slightly reworded form, is reproduced in Table I. In essence they prefer the term osteoblastoma as representing the neoplastic nature of the lesions and their cell of origin. They avoid the qualification "benign" as being both redundant and possibly misleading, on the basis of some rather aggressive recurrences and the occasional arguable report of malignant change.[24] Both the circumscribed and genuine osteoblastomas have cortical medullary and periosteal forms and the distinction between circumscribed and genuine is based largely on size. Schajowicz and Lemos[22] also introduced a third category, that of multifocal osteoblastoma, to account for occasional reports of somewhat bizarre cases.[15]

Diagnostic Criteria and Illustrative Cases

The University of British Columbia bone tumour registry has listed 32 conventional osteoid osteomas and 11 osteoblastomas. Cortical and medullary (cancellous) forms of osteoid osteoma were included but periosteal forms were not. Nor did we acknowledge the one multifocal lesion previously reported as recurring osteoid osteoma by Dunlop, Morton and Elliott.[15]

Using the classification suggested by Schajowicz and Lemos,[22] these 43 cases are grouped as shown in Table II. Four osteoid osteomas were accordingly classified as circumscribed osteoblastomas of periosteal origin and one was classified as sclerosing multifocal osteoblastoma. The remaining 38 cases were retained in the categories of circumscribed osteoblastomas (27 cases) and genuine osteoblastomas (medullary or cancellous) (11 cases).

It is thus clear that, in most instances, the benign bone-forming lesions are included in the classical categories of osteoid osteoma or osteoblastoma. But the proof of the value of the new classification is established only by satisfaction of two criteria: first, whether this classification serves the purpose it was designed for and, second, whether that purpose is of practical value. The first of these criteria (whether the classification serves the purpose) is best evaluated by consideration of some of our borderline cases in more detail.

Case Reports

Case 1.—A 29-year-old woman complained of an ache with localized tenderness over a mass that was fixed to the mid-portion of the right fibula. Radiographs showed a sclerotic and lytic eccentric expansion of the fibular shaft. Histologic examination of the excised specimen was typical of osteoid osteoma.

COMMENT.—Histologically, this lesion appeared to be a benign osteoblastic tumour but, radiologically, we found it difficult in 1955 to call it osteoid osteoma. A diagnosis of benign osteoblastoma was considered at the time of Jaffe's[19] and Lichtenstein's[20] descriptions in 1956, but it did not seem to fit their criteria on the basis of size. Classification of this lesion becomes possible by Schajowicz and Lemos'[22] concept of circumscribed osteoblastoma or osteoid osteoma of *periosteal* origin.

Case 2.—An 18-year-old girl had had a painful, stiff and swollen, tender ankle for 3

TABLE I.—Classification of Schajowicz and Lemos (Modified)

Circumscribed osteoblastoma (formerly osteoid osteoma; nidus less than 2 cm)
Cortical, sclerosing
Medullary, cancellous
Periosteal
Genuine osteoblastoma (formerly benign osteoblastoma; nidus larger than 2 cm)
Medullary, cancellous
Periosteal
Cortical, sclerosing
Multifocal osteoblastoma
Medullary
Peripheral

TABLE II.—Reclassification of 43 Benign Osteoblastic Tumours (University of British Columbia Bone Tumour Registry)

Circumscribed osteoblastoma
Cortical (n = 14)
Medullary (n = 13)
Periosteal (n = 4)
Genuine osteoblastoma
Medullary (n = 11)
Periosteal
Cortical
Multifocal osteoblastoma
Medullary
Peripheral (n = 1)

years, which had been treated as tuberculous arthritis. Radiographs showed an area of radiolucence in the body of the talus with a faint sclerotic periphery but no central calcification. Histologic examination of the excised, soft, dark nidus showed florid osteoblastic activity with bone production and multinucleated giant cells. The original diagnosis was benign osteoblastoma.

COMMENT.—This case was previously reported as a benign osteoblastic lesion resembling osteoid osteoma.[12] We now believe this lesion is an osteoid osteoma (circumscribed osteoblastoma of cancellous origin, Schajowicz) with unusual features of hypertrophic synovitis[13] and distant hyperostosis.[11] Although the classification of Schajowicz and Lemos[22] is not essential for the categorization of this lesion, we believe that their broader concept of benign osteoblastic lesions permits an easier acceptance of this somewhat bizarre picture.

Case 3.—A 45-year-old man had noted pain and swelling in the right hand for 18 months; the treatment was excision of a ganglion. Six years later pain persisted and radiographs and histologic examination led to a diagnosis of osteoid osteoma of the base of the second metacarpal. The lesion recurred and, 18 months later, was excised a second time; however, it recurred with multiple foci of osteoid tissue in the same region after another 18 months. This third excision was followed 1 year later still by excision of a small soft-tissue nodule of osteoid tissue.

COMMENT.—This case was reported previously as a recurring osteoid osteoma.[15] It now seems clear, based on the description of Schajowicz and Lemos,[22] that this tumour represents a multifocal sclerosing osteoblastoma (multifocal osteoid osteoma); these authors described both medullary and juxtacortical (peripheral) forms.

Case 4.—A 15-year-old boy complained of pain in the left hip for several months, relieved in part by aspirin. Radiographs showed a 1.5-cm lytic lesion in the femoral neck; the lesion was excised. The microscopic pattern was typical of osteoid osteoma in some areas (Fig. 1a) with osteoid trabeculae and sparse stroma, but in others (Fig. 1b) the pattern was much more cellular and exuberant with frequent giant cells, more suggestive of osteoblastoma.

COMMENT.—The clinical history and radiographic appearance are clearly consistent with a diagnosis of osteoid osteoma, although the size of the lesion (1.5 cm) is in the range characteristic of giant osteoid osteoma (osteoblastoma) as originally described by Dahlin and Johnson.[17] We were intrigued by the

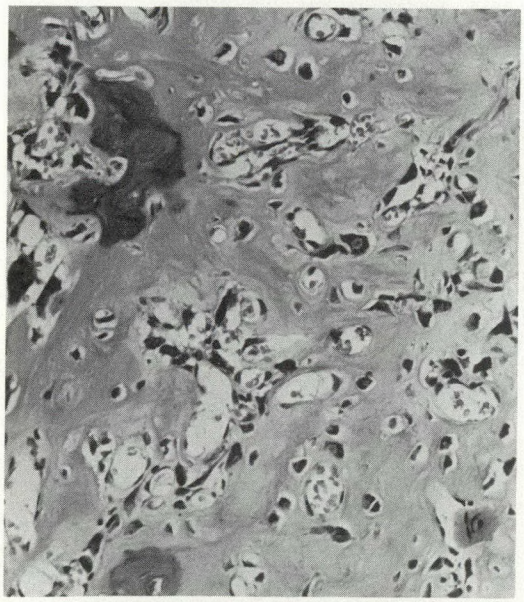

Fig. 1a

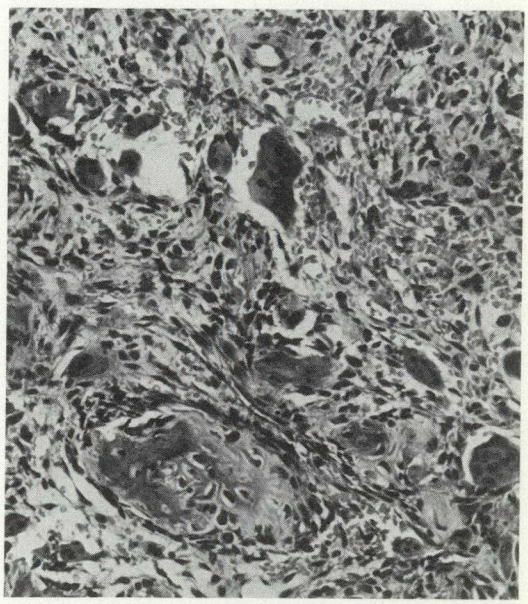

Fig. 1b

Fig. 1.—Case 4. (a) Dense irregular osteoid trabeculae suggest diagnosis of osteoid osteoma in this microscopic field. (b) In same section as in (a) microscopic appearance is clearly more cellular and vascular with multinucleated giant cells and osteoid trabeculae. Features of this area alone could be interpreted as those of osteoblastoma (hematoxylin and eosin, x 254).

variable histologic pattern of the lesion and we concluded that it illustrates criteria for each or both diagnoses. According to the terminology of Schajowicz and Lemos,[22] it would be referred to as a circumscribed osteoblastoma of medullary (cancellous) origin.

The second criterion (whether the new classification is of practical use) may best be considered by questioning the value of classifications in general. Their greatest value is probably as a teaching technique. Once the concept that they represent is properly understood and once one has knowledge of a description, the need for classification as such diminishes. Naming the lesion continues to be important for communication and for its implied treatment and prognosis, but constantly relating it to the total classification is probably unnecessary and can be awkward.

Initially we had registered in the bone tumour registry 32 osteoid osteomas and 11 osteoblastomas. Use of the new terminology, however, permitted us to classify the turnovers as 31 circumscribed osteoblastomas, 11 genuine osteoblastomas, and 1 sclerosing, peripheral, multifocal osteoblastoma. By applying and making use of the basic concept of the classification of Schajowicz and Lemos, we believe we have come to a greater understanding of benign osteoblastic tumours of bone—particularly their radiographic and microscopic appearances—but we find the new terminology at best awkward and at worst confusing.

Recently Dias and Frost[25] reached the same conclusion. In their view osteoid osteoma and osteoblastoma are variants of the same process, the nature of the reaction being determined by its location in bone. Accordingly they have proposed the terms *cortical osteoblastoma* (for osteoid osteoma) and *spongious osteoblastoma* (for benign osteoblastoma) recognizing also the usefulness of Schajowicz's categories *periosteal osteoblastoma* and *multifocal osteoblastoma*. Our only criticism of this approach is in the use of the awkward description *spongious,* for which we would substitute *medullary.*

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VASCULAR COMPARTMENT SYNDROMES*

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Summary: In a 5-year period (1968 to 1973) 33 cases of vascular compartment syndrome were seen. Seven case reports illustrate various etiopathogenetic factors in the development of vascular compartment syndrome. A review of the 33 cases has permitted discussion of the pathophysiology and clinical features of these syndromes, together with introduction of a clinical classification on which treatment is based. Mild cases may be treated by application of ice, elevation, and observation; for severe cases fasciotomy is the treatment of choice. Two techniques of fasciotomy are available: multiple skin incisions with fasciotomy between the incisions for single-compartment syndromes and extensive skin incisions over the length of the fasciotomy for multicompartment syndromes or severe single-compartment syndromes.

Résumé: Au cours d'une période de 5 années (1968 à 1973), nous avons vu 33 cas de syndrome du compartiment vasculaire. Sept cas ont permis d'illustrer divers facteurs étiopathogéniques du développement de ce syndrome. La revue globale des 33 cas a permis de discuter la physiopathologie et les caractéristiques de ces syndromes et, en outre, d'aboutir à une classification clinique sur laquelle repose le traitement. Les cas bénins peuvent être traités par l'application de glace, l'élévation et l'observation. Par contre, pour les cas sévères on choisit la fasciotomie. On dispose de deux techniques de fasciotomie: des incisions cutanées multiples avec fasciotomie entre les incisions dans le cas des syndromes à compartiment unique, et les incisions cutanées multiples sur toute la longueur de la fasciotomie dans les syndromes à compartiments multiples ou les cas sévères de syndromes à compartiment unique.

ONE of the most important yet neglected areas in the management of trauma is the recognition and prompt treatment of vascular compartment syndromes. The classic description of such a syndrome is that of Volkmann,[1] who noted ischemic contracture in the lower leg after the application of constricting bandages. Commonly, Volkmann's ischemic contracture is associated with supracondylar fractures of the humerus and resultant ischemia to the flexor compartment of the forearm, but this entity is only one of several vascular compartment syndromes. Others are the isolated anterior, the isolated posterior and the multicompartment syndromes in the lower extremity.[2-8]

In this paper we provide representative case reports of examples of these syndromes and discuss the pathophysiology, clinical features, classification and treatment of vascular compartment syndromes. A retrospective study of vascular compartment syndromes in 33 cases seen during the 5-year period from 1968 to 1973 was the basis of this review.

CASE REPORTS

Case 1.—A 26-year-old man was admitted to hospital in Moose Factory, Ont. after being rescued from James Bay during a storm. His legs had been immersed in the water for 16 to 20 hours. On admission, both legs were cold and swollen. Shock was treated by administration of intravenous fluids. He was then transferred to the Victoria Hospital, London, Ont. in renal failure. Approximately 36 hours after rescue his legs were grossly swollen, pulseless and anesthetic. There was no pain on passive toe movement. He was still toxic 36 hours later despite renal dialysis. Fibulectomy and fasciotomy were performed. All four lower extremity compartments were decompressed through the bed of the excised fibula. His condition deteriorated and, 8 days after admission, left below-knee amputation was performed. The entire right anterior compartment gradually sloughed but this leg was saved.

At the time of discharge there was no active dorsiflexion of his toes, only slight plantar flexion, and decreased sensation on the dorsolateral aspect of his right foot. At present he has a right foot-drop brace and a left below-knee prosthesis.

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COMMENT.—This is an example of multi-compartment vascular syndrome due to immersion limb cold injury.

Case 2.—A 19-year-old man was seen in the emergency department 1½ days after "jumping over a high fence". The right leg was swollen and tender over the entire anterior compartment. There was pain on passive plantar flexion of the toes, and muscle testing revealed zero power in the extensor hallucis longus and tibialis anterior muscles.

The anterior compartment was decompressed through multiple skin incisions, the fascia being incised throughout its length. Delayed primary closure of the skin incisions occurred on day 5, and this was followed by anterior compartment functional recovery.

COMMENT.—This example of isolated anterior compartment syndrome was due to indirect soft-tissue injury.

Case 3.—A 23-year-old man sustained a fracture of the left radius and ulna in a traffic accident. He was referred to the Victoria Hospital, London, Ont. 15 days after the accident. His arm was in a circular plaster cast; contracture of the wrist and fingers was noted. Fasciotomy was not performed because of the 15-day interval between fracture and diagnosis. After 4 months he still had a persistent flexion contracture of his wrist and fingers. Because of this, radical excision of both superficialis and profundus muscles and neurolysis of median and ulnar nerves were performed. Reconstructive surgery on the hand was performed subsequently.

COMMENT.—In this case Volkmann's ischemic contracture of the forearm followed fracture of both bones of the forearm—possibly a more common cause than supracondylar fracture of the humerus.

Case 4.—A 20-year-old man sustained closed fractures of his left tibia and fibula during a baseball game. These were treated with open reduction and Lottes' nail fixation. Four hours later he complained of pain, numbness and loss of active toe motion. An anterior compartment fasciotomy alone was performed.

Two months later he was seen because of a fixed equinovarus foot with claw toes. He required reconstructive surgery and treatment of trophic ulceration because of failure of recognition of a posterior compartment syndrome.

COMMENT.—This is an example of an unrecognized posterior compartment syndrome resulting in reconstructive surgery and treatment of trophic ulceration.

Case 5.—A 19-year-old man, who was involved in a motor vehicle accident, sustained an open fracture of his right femur, an open fracture of his right tibia and fibula, and disruption of the femoral artery at the fracture site in the femur. Primary repair of the femoral artery by end-to-end anastomosis was carried out, followed by debridement of the areas at both fracture sites and extensive fasciotomy of the anterior, lateral and both posterior compartments. The degree of herniation of muscle through the fascia was impressive.

Six days later delayed primary closure of the wounds was performed, but bulging through the anterior fasciotomy incision was even more obvious and the incision could not be closed. It required split-thickness grafts 5 days later. Despite these measures, foot-drop was noted temporarily after grafting, but there was no evidence of posterior or lateral compartment problems.

COMMENT.—This case demonstrates the need for fasciotomy in fractures associated with arterial injury.

Case 6.—A 17 year-old boy suffered from recurrent patellar subluxation requiring a Hauser stabilization procedure. On the 3rd day after operation his foot was blue and he had a mild foot-drop. The cast was removed and the leg elevated. The peroneal nerve, explored on the 4th postoperative day, appeared to be normal.

Five months after surgery, strength in the extensor hallucis longus, peronei and tibialis anterior muscles was greatly diminished. The Muscle biopsy revealed ischemia, and electromyographic studies and nerve conduction confirmed this. The patient has been able to walk without a foot-drop brace.

COMMENT.—This is a well-recognized complication following reconstructive knee surgery. Five cases of the identical presentation following the Hauser procedure were discussed at the American Academy of Orthopaedics meeting in 1973.[9]

Case 7.—A 17-year-old girl took an overdose of propoxyphene hydrochloride (Darvon) and, while being treated in the emergency department, suffered severe grand mal seizures

with violent tonic muscle contractions. Orthopedic consultation was requested 24 hours later because of swelling of the anterior compartment of both legs. Treatment by application of ice and elevation for 1 hour was not successful and, 30 hours after admission, fasciotomy was carried out through multiple skin incisions.

The patient now has a power of 4 in all muscle groups of the anterior compartment except the extensor hallucis longus, which has a power of 2.

COMMENT.—This is an example of an unusual presentation of isolated anterior compartment syndrome following grand mal seizure with violent tonic muscle contraction.

Pathophysiology

Several theories have been postulated for the cause of the resultant contractures. In 1881, Volkmann[1] described arterial occlusion and its sequelae as the cause. Brooks[10] in 1922 described venous obstruction, and Jepson[3] in 1926 implicated external compression as the major factor responsible for the syndrome. Others have implicated arterial spasm,[11] capillary paralysis[12] and peripheral nerve injuries.[13]

The single factor common to these syndromes is interruption of the arterial supply.[2, 4, 14-18] The initial injury causes an arterial lesion or hemorrhage in strictly confining osseofacial compartments. This results in edema, swelling and significant increases in tension within these confined compartments. If the degree of trauma is slight, the process will often resolve, but if it is severe the increase in tension impairs venous return, produces more swelling and edema and reduces arterial flow. All of these factors lead to ischemia. The pathophysiologic factors of importance in vascular compartment syndromes are depicted diagrammatically in Fig. 1.[5]

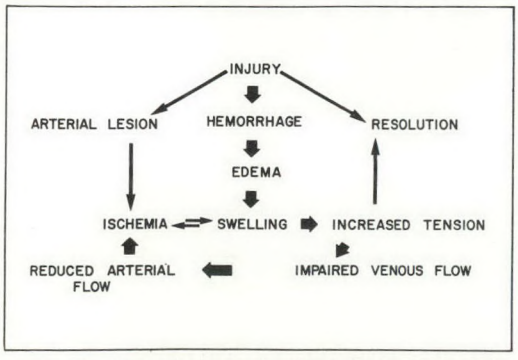

Fig. 1.—Factors in pathophysiology of vascular compartment syndromes (modified from McQUILLAN WM, NOLAN B: Ischemia complicating injury. *J Bone Joint Surg* [*Br*] 50: 482, 1968).

Rorabeck and Macnab[19] investigated the isolated anterior compartment syndrome and gave arteriolar occlusion as the cause for the ischemia. Their experimental evidence showed that a pressure of only 30 to 50 mm Hg was necessary to cause occlusion of nutrient arterioles to muscle.

Persistent, severe, or complete ischemia is the result of interruption of the arterial or arteriolar supply and eventually leads to myonecrosis, fibrosis and the resultant contracture. Occlusion of vessels in the perineurium of the peripheral nerves results in the same fibrotic mechanism.[20]

Clinical Features

The classic clinical warnings of ischemia are pain, pallor, absence of pulses, puffiness, paresthesia and paralysis. The most reliable sign is painful limitation of movement of either fingers or toes.[5, 8, 18] The pain is aggravated by passive movements that stretch the affected muscles. Examples of such movement are extension of the fingers causing pain in the flexor compartment of the forearm with classic Volkmann's ischemia and flexion of the toes with isolated anterior compartment syndrome of the lower extremity.

Evaluation of the peripheral circulatory status is not useful in monitoring these syndromes because the pulses are often present and the skin is kept warm by an adequate collateral circulation.[5, 7, 8, 18]

Classification

To facilitate selection of the method of treatment we have subdivided the vascular compartment syndromes into three classes (I [mild], II [moderate] and III [severe]) with respect to pain on passive movement, swelling, weakness and sensation. Table I summarizes the distribution of vascular compartment syndromes according to anatomical localization and their severity among the 33 patients.

TABLE I.—DISTRIBUTION AND SEVERITY OF VASCULAR COMPARTMENT SYNDROMES

Anatomic basis of syndrome	Class I (mild)	II (moderate)	III (severe)	Total no. of patients
Upper extremity:				
Volkmann's ischemia of forearm	0	2	4	6
Lower extremity:				
Anterior compartment	3	4	0	7
Posterior compartment	3	6	0	9
Multicompartment	0	6	5	11
Total	6	18	9	33

TREATMENT

The treatment is relatively simple once the diagnosis has been made. In class I the physician can temporize with the application of ice, elevation of the limb and close observation of the patient. Close observation is essential because the condition can deteriorate rapidly.

If the condition does not resolve or if it worsens, fasciotomy is the treatment of choice. Certainly, if the process is not resolving, conservative management, epidural anesthesia and sympathectomy are to be condemned, whatever the class.[6, 7, 17]

There are two chief techniques of fasciotomy (Fig. 2):

1. Multiple skin incisions and extensive fasciotomy between the incisions is most often selected in cases of single-compartment syndromes.

2. An extensive skin incision over the entire length of the fasciotomy is recommended in the management of multiple-compartment syndromes or severe single-compartment syndromes. The skin incisions are left open, and are closed on a delayed, primary basis or are skin grafted (Fig. 3).

Once the impressive herniation and bulging of the muscle mass from its compartment after fasciotomy have been seen, the need for the procedure is readily apparent. The technique of fibulectomy and fasciotomy as recommended by Ernst and

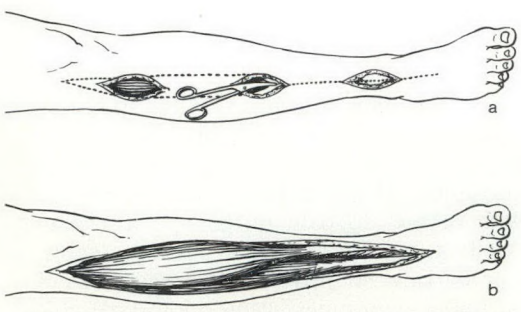

Fig. 2.—Methods of fasciotomy. (a) Multiple skin incisions and fasciotomy between incisions. (b) Extensive skin incision and fasciotomy.

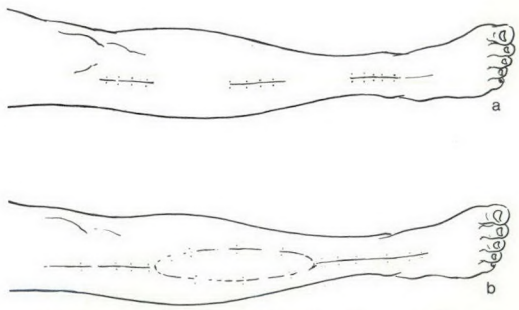

Fig. 3.—Method of delayed primary skin closure. (a) Suture alone. (b) Suture and split-thickness skin graft.

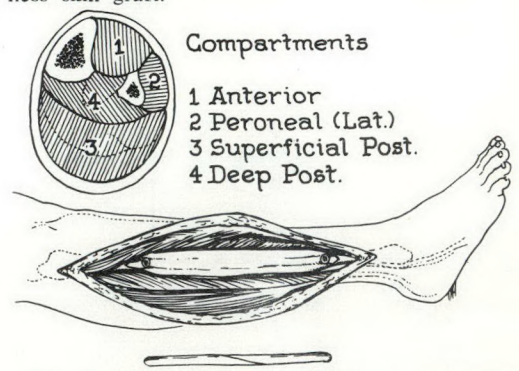

Fig. 4.—Access to all four lower extremity compartments after fibulectomy (modified from ERNST CB, KAUFER H: Fibulectomy-fasciotomy: important adjunct in management of lower extremity arterial trauma. *J Trauma* 11: 365, 1971).

Kaufer[2] is ideal for class III multicompartment lesions because it provides access to all four lower extremity compartments through the bed of the excised fibula (Fig. 4).

Ischemic compartment syndromes in the upper limbs are largely confined to children, and those in the leg are more common in adults.[4]

The incidence of posterior compartment syndrome following tibial fractures approaches 10% in some series.[21] Because severe deformity and disability may develop in patients who receive no specific treatment, the following recommendations concerning indications for fasciotomy merit emphasis.

Indications for Fasciotomy

1. Fracture associated with arterial injury: The high incidence of vascular compartment syndrome following fracture with arterial injury makes fasciotomy an absolute necessity.[4, 6, 16, 17]

2. Arterial injury alone: If the patient has an isolated arterial injury and the interval between injury and operation is 4 to 6 hours, fasciotomy is indicated.[14, 15]

3. Extremity fractures with extensive soft-tissue injury: Extensive soft-tissue injury associated with both closed and open upper and lower extremity fractures warrants fasciotomy because this procedure is simple and safe.[5, 8, 18]

4. Diagnosis of class II or III vascular compartment syndromes.

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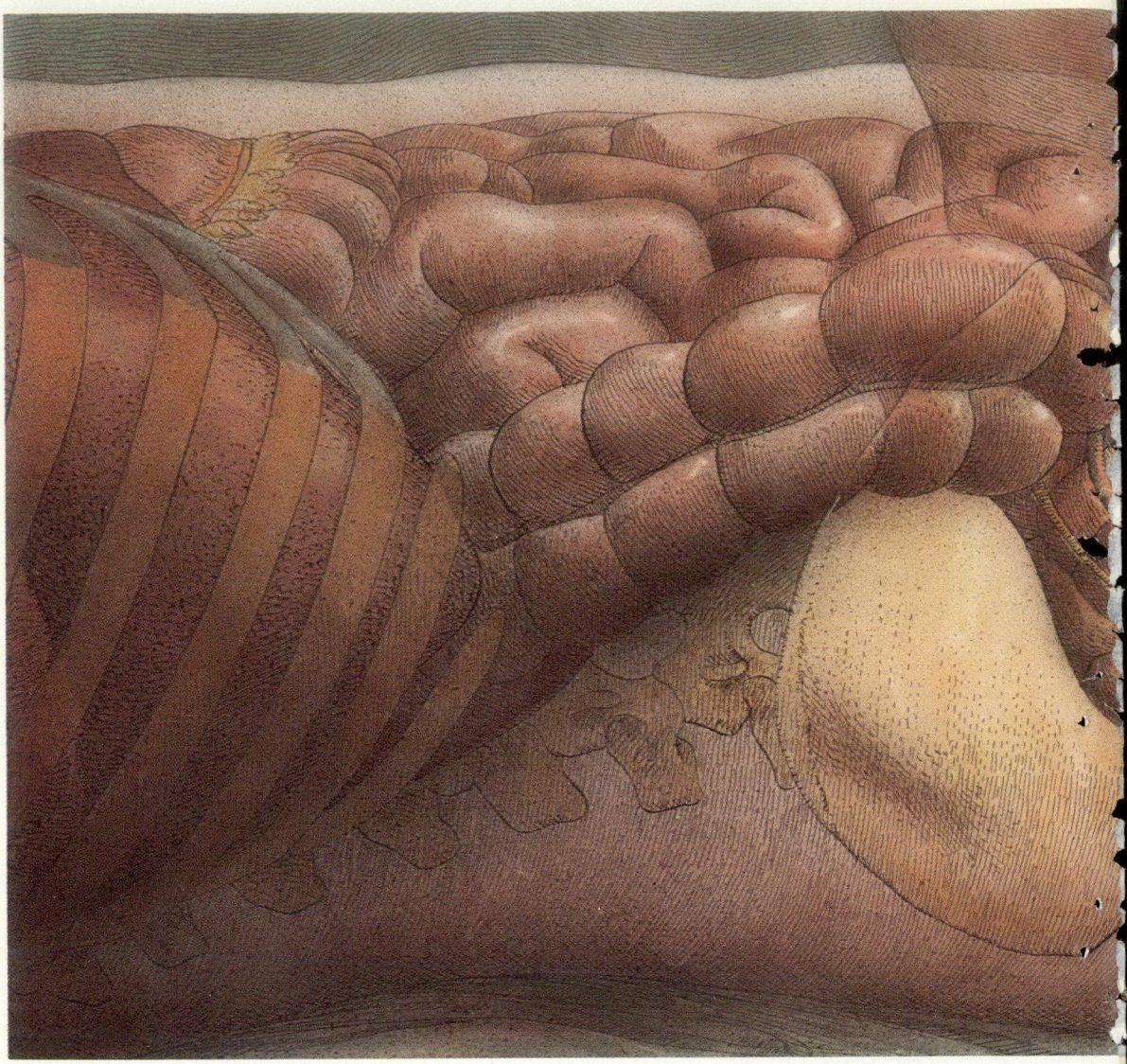

an emerging problem.

"Bacteroides species are often overlooked as a cause of serious infection both by clinicians and microbiologists. They are most commonly associated with intra-abdominal and pelvic sepsis following gastrointestinal surgery."

Tracy, O., et al. (29 Jan.'72).
Brit. med. J., p. 280.

"Our experience with this series of seriously ill patients provides clinical confirmation to complement recent in vitro evidence that clindamycin is the antibiotic of choice for use in bacteroides infections. Not only was the response in 17 of the 18 patients favourable, but in several it was dramatic."

Haldane, E.V. and van Rooyen, C.E. (1972).
C.M.A.J., p. 1177.

GLIMPSES OF SURGICAL HISTORY: B FOR BLOOD TRANSFUSION

D. A. E. SHEPHARD

Blood, with its rich symbolism, has long seemed magical but the history of BLOOD TRANSFUSION is relatively recent. Man first had to conceive the idea of injecting substances into the body and to formulate the concept of the circulation. The 17th century was crucial. Libavius (1615) was one of several to suggest blood transfusion but the seminal event was the discovery of the circulation by Harvey (1616). An astronomer-architect, Wren, injected drugs—and blood—into animals in 1656; a physician-anatomist, Lower, transfused blood from one animal to another in 1665; and a philosopher-mathematician-physician, Denys, transfused blood into a human being in 1667. Denys' patient received about 270 ml of lamb's blood; but another of his patients died after a transfusion. Transfusion lost favour, perhaps fortunately because the technique was not understood and was certainly misused: it was used for conditions as varied as lung disease, bowel disorders, senility and insanity.

Its reinstatement was the work of the English obstetrician, Blundell. Puerperal hemorrhage dismayed him. His experiments demonstrated two points: death from hemorrhage could be prevented by tranfusion of blood from animals of the same species, and successful transfusion required species-compatible blood. Blundell was the first to transfuse human blood into humans (1818). He also showed that passage through instruments did not damage blood and that air bubbles need not be harmful.

Coagulation, phlebitis and reactions remained problematical. Coagulation was overcome to some extent with Aveling's rubber bulb to expedite blood flow (it could also be carried in the pocket from patient to patient). Defibrinated blood (even when a wire egg beater and a hair sieve were used) also helped. Another idea was the use of sodium phosphate as an anticoagulant (but Braxton-Hicks found that it was toxic).

Once again the technique declined. By 1873 obstetricians regarded transfusion as a desperate measure. Again it was being misused: all sorts of patients, including "the burnt, the uremic, the syphilitic and the mad" received blood — even animals' blood.

The final victory came with the 20th century. Landsteiner and also Shattock detected agglutinins and isoagglutinins; Landsteiner, and others, also identified the major blood groups; Kimpton and Brown paraffined containers; Lewisohn and others preserved blood with sodium citrate; and Fantus made blood banking possible. These techniques, as well as the use of heparin, finally made complex operations possible and saved a myriad lives.

ESOPHAGEAL RECONSTRUCTION: AN EXPERIMENTAL APPROACH TO THE CONTROL OF REFLUX AFTER ESOPHAGEAL RESECTION*

R. D HENDERSON, MB, FRCS[C], K. FUNG, MD, P. DUBE, FRCS(Eng) and G. MARRYATT, RNA

Summary: A study of the properties of replacement gastric tubes and colonic segments, and their use in the prevention of reflux after esophageal resection indicates that, in order to prevent reflux, these tubes must be maintained in a subdiaphragmatic position. Gastric tubes have a higher intrinsic pressure barrier than colonic tubes—a 2.5- to 6-cm segment prevents reflux and the tube maintains a pressure barrier 10 cm H_2O higher than stomach pressure, whereas colonic segments require 12 cm of subdiaphragmatic length to control reflux and maintain a pressure barrier only 2 cm H_2O above gastric pressure. Removal of the intrinsic pressure barrier by myotomy allows free reflux in tubes that previously had prevented reflux.

Résumé: Après avoir étudié les propriétés des tubes de remplacement de l'estomac et du côlon et leur utilisation pour prévenir le reflux après résection de l'œsophage, nous avons constaté que, pour remplir leur but, ces tubes doivent être maintenus en position sous le diaphragme. Les tubes gastriques ont une barrière de pression intrinsèque plus élevée que les tubes du côlon: un segment de 2.5 à 6 cm empêche le reflux et le tube maintient une barrière de pression de 10 cm H_2O plus forte que la pression gastrique, tandis que, pour enrayer le reflux, les segments du côlon doivent avoir une longueur sous-diaphragmatique de 12 cm et ne maintiennent une barrière de pression, par rapport à la pression gastrique, que de 2 cm H_2O. La suppression de la barrière de pression intrinsèque par myotomie permet le reflux libre dans les tubes qui, auparavant, empêchaient le reflux.

AFTER esophageal resection, some form of replacement surgery is necessary. Various approaches have been tried and at present replacement by stomach[1-6] and by colon[7-9] are the most popular methods. Of the well-recognized problems in replacement surgery, the long-term effect of gastric reflux upon the replacement organ is particularly important.

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At 6 months after the use of stomach as a replacement organ, the incidence of peptic stricture has been reported as 27%.[10] Anderson and Randolph[11] used a gastric tube to replace the esophagus, and reported ulceration and perforation in the tube segment. In colonic replacement of the esophagus, reflux is less often a problem, but peptic ulcers of the colon have been reported,[12, 13] and some experimental data suggest that the colon mucosa is sensitive to gastric juice irritation.

The present study was designed to determine the pathophysiologic properties of gastric tubes and colonic segments, and to investigate how these could be used to prevent reflux in experimental esophageal reconstruction.

GASTRIC TUBE STUDY

Dogs in this study were prepared by excision of the lower 10 cm of esophagus and replacement of this segment by a gastric tube of the same circumference as the esophagus. The tube was taken from the greater curvature of the stomach and constructed over a metal cylinder (circumference 6.5 cm, equivalent to a no. 50 French bougie). The constructed tube was anastomosed to the distal esophageal stump. All dogs had a vagotomy and pyloroplasty.

The animals were trained to accept esophageal motility tubes while fully conscious and each dog was studied before and after surgery. Preoperatively, three manometric studies were performed using a three-tube system of polyethylene PE 240 tubes bound together with side openings 5 cm apart. Constant water infusion was maintained by a 2202 Harvard pump. Statham P23De strain gauges were used as sensing devices and a 1508 Honeywell ultraviolet visicorder recorded the pressure.

After 2 weeks' convalescence, each dog had three manometric studies. Barium cinematographic and combined radiologic, manometric and pH studies were done to relate pressure changes in the gastric tube to its anatomical position.

Intra-abdominal Versus Intrathoracic Gastric Tubes

After the basic operation, the gastric tube was placed in one of three positions as follows (Fig. 1):

1. In Group I (three dogs), a 6-cm gastric tube was maintained below the diaphragm and wrapped two-thirds around by gastric fundus (fundal plication).
2. In Group II (four dogs), a 6-cm segment of gastric tube was placed below the diaphragm without gastric fundal plication.
3. In Group III (three dogs), a 6-cm gastric tube was placed entirely within the chest with the point of junction between the tube and stomach at the diaphragmatic level.

All preoperative manometric studies showed normal canine esophageal motor function.

The results in Group I and II dogs (seven dogs) were identical. There was no radiologic or pH evidence of reflux with an intra-abdominal tube segment of 6 cm. Manometrically, the tube segment had a zone of elevated pressure of 16 cm H_2O, the mean gastric pressure was 6 cm H_2O and the mean esophageal pressure was -2 cm H_2O; a pressure barrier of 10 cm H_2O between gastric tube and stomach was maintained (Fig. 2, Table I).

Radiologically, Group III dogs (three) showed free reflux at all times. During combined radiologic and manometric studies it was possible to produce free reflux by abdominal compression, which simultaneously raised esophageal pressure and produced a fall in esophageal pH. The manometric pattern seen in this group of dogs was exactly the same as in the preceding groups except that there was a definite elevation of esophageal pressure from -2 to $+18$ cm H_2O.

This study showed that a 6-cm segment of subdiaphragmatic gastric tube prevented reflux. We now believed it necessary to examine further the length of gastric tubes that would prevent reflux and for this purpose gastric tubes of varying length were constructed.

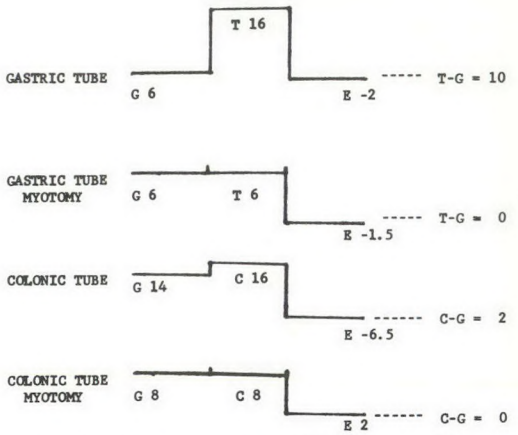

Fig. 2.—Average manometric pressures in gastric and colonic tube segments and average gastric (G) and esophageal (E) pressures at each stage of study. Comparison of tubal pressure (T) minus gastric pressure (G) (T - G) shows that normal gastric tube has pressure barrier of 10 cm H_2O. After myotomy T - G becomes 0. In colonic tubes, tubal pressure (C) minus gastric pressure (G) (C - G) is 2 cm H_2O and after myotomy C - G becomes 0.

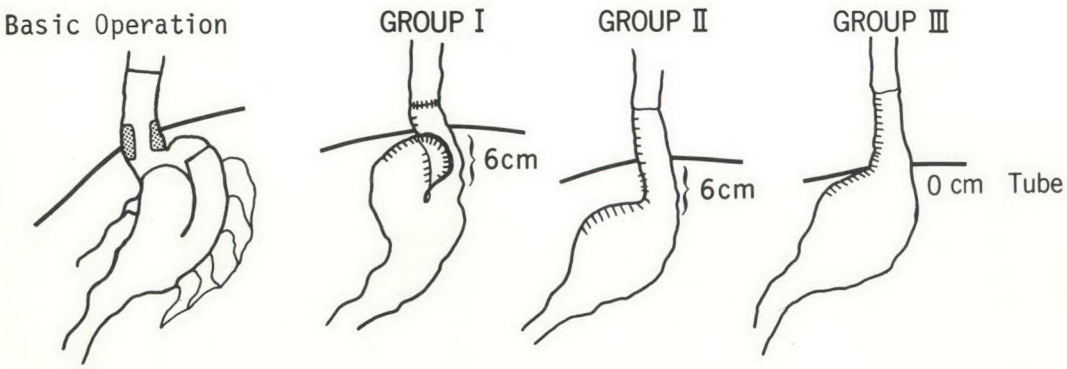

Fig. 1.—Basic operation and placement of gastric tube in Groups I, II and III. In Group I, 6 cm of tube is maintained below diaphragm and wrapped with stomach. In Group II, 6 cm of tube is maintained below diaphragm without gastric wrap. In Group III, gastric tube is entirely intrathoracic. Note acute angle in Group I and obtuse angle in Group II.

Subdiaphragmatic Gastric Tube Lengths

In six dogs, gastric tubes of varying lengths were constructed. One dog had a 4-cm tube, two dogs had a 3-cm tube and two had a 2.5-cm tube. Study of these dogs was carried out as in stage I and showed the normal tubal pressure and no evidence of radiologic, manometric or pH reflux. One dog had construction of a 2-cm tube and showed free reflux demonstrated by all techniques.

Myotomy—Subdiaphragmatic Gastric Tubes

Having demonstrated that subdiaphragmatic tubes prevented reflux and that these tubes by themselves had an intrinsic pressure, we believed it was necessary to examine the properties of the tube by myotomizing the gastric tubes. Five of the previously studied dogs were selected for myotomy of the subdiaphragmatic gastric tube. These dogs had tubes 6, 6, 4, and 3 and 2.5 cm in length and had been fully studied to demonstrate that they did not have reflux. A second operation was performed using a transabdominal approach, and the intra-abdominal segment of the tube was myotomized from the level of the diaphragm to its point of junction with the stomach. After myotomy of the intra-abdominal tube segments, the dogs with one exception freely refluxed radiologically, manometrically and by pH studies. The one dog (with a 3-cm tube) without reflux, at autopsy was shown to have an incomplete myotomy.

Manometrically, there was a reduction in pressure of the tube segment with total elimination of the pressure barrier from the gastric tube to stomach (Fig. 2).

Colonic Segment Study

This same experimental model has been used to study the properties of colonic segments used to replace the lower esophagus. The dogs were again studied manometrically and found to have normal preoperative motor function.

The dogs were prepared preoperatively with neomycin. For exposure a short thoracoabdominal incision was used. Colonic segments were vascularized from the ascending branch of the left colic artery. The distal 10 cm of esophagus was excised, and vagotomy and pyloroplasty were performed. End-to-end anastomosis and cologastric isoperistaltic anastomosis were constructed. The colonic segments of varying lengths were positioned differently in the various dogs: in three, a 6-cm colonic segment was placed in a subdiaphragmatic position; in three dogs the segment was above the diaphragm and in two dogs a 12-cm colonic segment was positioned supradiaphragmatically.

Reconstruction by any of these three methods produced identical results. All dogs had free radiologic and manometric reflux. The manometric studies showed an average gastric pressure of 14 cm H_2O and a low basal tone in the colonic segments of 16 cm H_2O. There were superimposed colonic segmental contractions of up to 20 cm amplitude and of 30 to 60 seconds' duration. The pressure barrier from colon to stomach averaged 2 cm H_2O (Fig. 2).

Despite prolonged continuous manometric studies, there was no evidence of peristaltic colonic motor activity.[14, 15] When boluses of water and 0.1N HCl were injected, the colonic segment responded by a slow pressure rise followed by a sharp nonperistaltic pressure wave, which corresponded to the pressure wave of esophageal peristalsis.

Combined fluoroscopic and manometric studies showed that the injected bolus, made

TABLE I.—Average and Range of Pressures (cm H_2O) in Tube Segments and Tubal Barrier to Reflux*

	Stomach		*Tube*		*T − G*	
	Average	*Range*	*Average*	*Range*	*Average*	*Range*
Gastric tube	6	2 — 10	16	7.5 — 25	10	7.5 — 20
Gastric tube myotomy	6	0 — 12	6	0 — 12	0	1 — 1.3
Colonic tube	14	8 — 20	16	10 — 20	2	1 — 3
Colonic tube myotomy	8	4 — 10	8	4 — 10	0	1 — 1

*Minimum of three studies per dog.

radiopaque by addition of barium, was forced back into the distal esophagus by colonic contraction waves and the bolus then triggered esophageal peristalsis, which cleared it through the colonic segment and into the stomach.

Having found that a 6-cm subdiaphragmatic colonic segment did not control reflux, we then constructed a 12-cm subdiaphragmatic colonic segment in three animals. They showed no radiologic or manometric evidence of reflux. The manometric pressures and motor function in these dogs were identical to those seen in the earlier studies.

As a final stage of study, the three dogs with 12-cm subdiaphragmatic colonic segments that had been proved to be competent were then fully myotomized from the level of the diaphragm to the point of junction with the stomach. All dogs in this group showed free radiologic, manometric and pH reflux after myotomy. There was a complete loss of the pressure barrier from colon to stomach. The average colonic and gastric pressures in these dogs were 8 cm H_2O.

Discussion

We have shown that a gastric tube of esophageal diameter maintained a pressure barrier of 10 cm H_2O above gastric pressure. When this tube is placed above the diaphragm, the same pressure barrier exists but free reflux occurs. If the tube is maintained 2.5 to 6 cm below the diaphragm, reflux is prevented. Myotomy of the subdiaphragmatic tube segment abolishes the pressure barrier from tube to stomach and allows free reflux (Fig. 2).

Using colonic segments to replace the lower esophagus we found that a 6-cm segment of colon above or below the diaphragm did not prevent reflux. The cologastric pressure barrier was only 2 cm H_2O. When the length of colon was increased to 12 cm the subdiaphragmatic colonic segment prevented reflux while a supradiaphragmatic segment still allowed free reflux. Myotomy of the subdiaphragmatic colon totally abolished its pressure barrier and again free reflux occurred.

The gastric tubes and colonic segments appear to act as an effective pressure barrier to reflux in that, if sufficient length of tube is maintained below the diaphragm, reflux is prevented. The mechanism of the antireflux barrier provided by these tubes probably is more complex than simple maintenance of a pressure barrier, but the pressure barrier is important because free reflux recurs after ablation by myotomy. We conclude that two of the major factors in preventing reflux are the pressure barrier and tubal length. In the gastric tube the pressure barrier is higher, and reflux can be prevented by a 2.5-cm tube. When the gastric tubal barrier is ablated by myotomy, free reflux occurs, even with a 6-cm tube. In the colonic segment the tubal pressure is low and a 12-cm segment of colon is necessary to prevent reflux. Reflux again occurs in the colon when the pressure barrier is ablated by myotomy.

We believe that the antireflux properties of the tube depend upon its subdiaphragmatic position (Fig. 3). When intraperitoneal pressure is increased, this acts equally upon the stomach and the subdiaphragmatic tube. Any increase in gastric pressure will be counterbalanced by a similar increase in tubal pressure. When the tube itself maintains a constant tone, then this pressure barrier remains intact and acts to prevent reflux from stomach to esophagus. When the

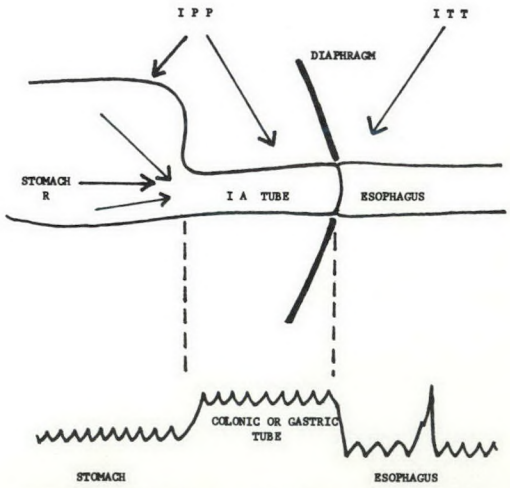

Fig. 3.—Antireflux mechanism of tubes. Tube segment, either gastric or colonic, is interposed between body of stomach and esophagus. Tone of tube segment, supported by intraperitoneal pressure (IPP) counterbalances gastric reflux pressure (R). If tube segment is intrathoracic then it loses support of IPP and tone is no longer sufficient to prevent reflux. ITT = intrathoracic pressure.

tube is placed in the chest, there is no counterbalancing pressure on the tubal segment so that increased intraperitoneal pressure will independently raise gastric pressure. When gastric pressure is raised sufficiently, it can overcome the antireflux pressure barrier of the constructed tube and reflux will then occur. Subdiaphragmatic myotomy of the gastric or colonic tubes reduces the tone and as a result there is no effective pressure barrier from stomach to esophagus. Reflux under these circumstances can freely occur (Fig. 3).

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MEDICAL PERSPECTIVES IN CORONARY ARTERY SURGERY

A feature of the history of coronary artery surgery is the persuasion with which proponents and opponents have proffered their viewpoints. A balanced view of the medical perspectives of coronary artery surgery is that of W. B. Dunkman and his colleagues (Ann Intern Med *81: 817, 1974*). *They conclude that although a "plausible rationale and dramatic symptomatic relief have resulted in widespread acceptance of coronary artery surgery...uncertainties abound...sufficient to warrant careful, critical appraisal and to caution that bypass grafting should* not *be done on all patients...The thesis is untenable that surgery is warranted whenever an anatomic lesion is discovered that is technically amenable to bypass with an acceptable mortality."*

Evaluation of the results of coronary artery surgery is complex. The natural history of coronary artery disease and the effects of medical management on outcome must be considered. Data must not be interpreted with invalid comparisons; for example, application of results of treatment of chronic stable angina (for which surgery offers better long-term results than those of nonsurgical treatment) to unstable angina (for which predictions are less clear), extrapolation of results in large and experienced centres to those in smaller and less experienced ones, and translation of beneficial symptomatic results into favourable effect on mortality. The type of coronary artery disease must be considered—whether it is chronic stable angina, unstable angina, postinfarction angina, Prinzmetal's angina, main left coronary artery disease, or acute myocardial infarction. And etiologic factors such as hypertension, electrocardiographic patterns, congestive heart failure, sex, age, smoking, serum cholesterol and physical inactivity must not be forgotten.

Surgery may be useful in certain cases of chronic stable angina, unstable angina under certain circumstances, uncontrolled Prinzmetal's angina, main left coronary artery disease, complicated acute myocardial infarction, asymptomatic coronary artery disease, and valve replacement with coexisting coronary artery disease. This presupposes skilful selective coronary angiography and equally skilful surgery. And today's results must be interpreted in light of the evolutionary stage of surgical treatment of coronary artery disease. Revisions of conclusions will be necessary for some time to come.

METHYLMETHACRYLATE CEMENT: ITS CURING TEMPERATURE AND EFFECT ON ARTICULAR CARTILAGE

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Summary: The increasing use of methylmethacrylate in orthopedic surgery makes it desirable to determine whether the curing temperature of methylmethacrylate is high enough to cause bone necrosis and whether methylmethacrylate damages articular cartilage. Studies in dogs showed that methylmethacrylate plug temperatures ranged from 95 to 107°C and that temperatures at the cement-bone interface ranged from 50 to 95°. Curing temperatures therefore are high enough to cause necrosis of bone. Other studies revealed no harmful action of methylmethacrylate on articular cartilage. Fractures stabilized with methylmethacrylate can therefore be expected to heal provided the normal criteria of fracture management are fulfilled.

Résumé: Depuis que le méthylméthacrylate est employé de plus en plus en chirurgie orthopédique, il devient souhaitable d'établir si la température de guérison du produit est assez élevée pour causer une nécrose de l'os et si le produit risque de léser le cartilage articulaire. L'étude expérimentale chez le chien a permis de montrer que les températures atteintes par des chevilles de méthylméthacrylate variaient de 95 à 107°C et que les températures au niveau de la surface de contact entre le ciment et l'os variaient de 50 à 95°. Il s'ensuit que les températures de guérison sont assez hautes pour provoquer la nécrose osseuse. D'autres études n'ont pas révélé d'action nocive du produit sur le cartilage articulaire. On peut donc s'attendre à ce que les fractures stabilisées par le méthylméthacrylate guérissent à condition que soient réunis les critères normaux du traitement des fractures.

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In the last 5 years, the use of methylmethacrylate bone cement in orthopedic surgery has greatly increased, and its use will probably continue to expand. Despite its increasing application, the effects of methylmethacrylate on bone, cartilage and other organ systems are poorly documented. Charnley's monograph,[1] however, provides substantial information concerning the effects of methylmethacrylate on bone, and there are scattered reports on the effects of the free monomer on the cardiovascular system[2, 3] and on the ultrastructure of methacrylate.[4] Recently, a number of new uses have been found for bone cement—as an adjunct in the reconstruction of comminuted fractures near joints, as a buttress for plates used to fix intertrochanteric fractures, and as an aid in the treatment of pathologic fractures[5]—and in these circumstances the methylmethacrylate comes into fairly close apposition with articular cartilage. In comminuted intra-articular fractures the cement may actually come in contact with the joint or lie very close to the articular cartilage. Therefore, the following questions arise:

1. What effect has methylmethacrylate on articular cartilage?
2. Does damage occur during exothermic polymerization?
3. Is nutrition of the cartilage affected?
4. What influence will the rigid methacrylate in its subchondral location have on the physical properties of articular cartilage?

Mixture of the cement components leads to exothermic polymerization, and attempts have been made to investigate the heat produced. Charnley[1] reported temperatures of 90°C in samples the size of golf balls 4 to 8 minutes after curing, and Homsy[6] recorded a temperature of 80 to 100°C at the bone polymer interface a few minutes after implantation.

We investigated the curing temperature of methylmethacrylate, *in vitro* and *in vivo*, and its effects on articular cartilage.

METHOD

Curing Temperature of Methylmethacrylate

We first determined the curing temperature of methylmethacrylate *in vitro*. Holes (diameter, 11 mm) were drilled through the diaphysis of the tibia of adult dogs and thermocouples were inserted (Fig. 1). One electrode was placed in the centre of the diaphyseal hole (1), one at the edge of the hole (3), one 5 mm from the hole (5) and one some distance away (6). Reference electrodes (2 and 4) were placed in iced water. The electrodes were connected as follows: 1 to 2, 3 to 4, 5 to 6. Methylmethacrylate was then prepared and placed in the hole. The thermocouples were monitored through a Beckman multichannel recorder.

We then repeated the experiment *in vivo* with the femur of adult dogs, but the hole did not penetrate the medial cortex completely in order to prevent extrusion of cement subperiosteally opposite the point of insertion.

Effect of Methylmethacrylate on Articular Cartilage

We next studied the effect of methylmethacrylate on articular cartilage. The lateral femoral condyle of an adult dog was excised by means of a sagittal cut through the intercondylar notch lateral to the cruciate ligament to preserve the stability. The cut was extended proximally for 5 cm and then taken laterally. The lateral collateral ligament was divided and the condyle was excised. All cancellous bone and as much subchondral bone as possible was removed with a dental burr to create a thin shell of cartilage in which both patellofemoral and femorotibial articulations were represented. The shell was filled with methylmethacrylate, replaced and fixed to the medial condyle by two cancellous screws. The dogs were allowed to bear weight fully postoperatively; there were no adverse effects and, at 6 weeks, all the dogs walked normally and experienced no discomfort. The dogs were then killed. The affected extremities were removed and the specimens were fixed in buffered formalin phosphate. The methylmethacrylate was dissolved out with the aid of a 1:1 mixture of methylmethacrylate monomer and 100% ethyl alcohol. The specimens were processed and stained with hematoxylin and eosin, toluidine blue or WHO stain.

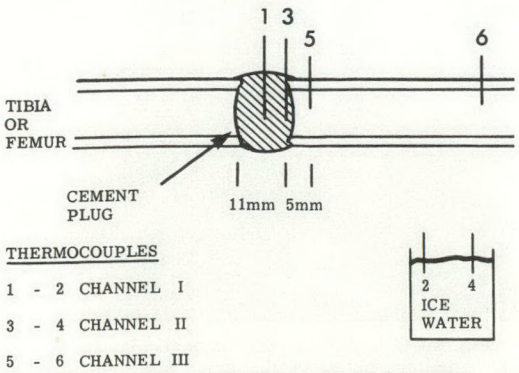

Fig. 1.—Arrangement of thermocouples.

RESULTS

Curing Temperature

Temperatures recorded *in vitro* from the thermocouple located within the cement plug (thermocouple 3 to 4) ranged from 95 to 100°C and those recorded at the cement-bone interface (thermocouple 1 to 2) ranged from 50 to 70°C. The *in vivo* readings within the cement plug were similar to those *in vitro*, 104 to 107°C; at the bone-cement interface, temperatures ranged from 75 to 95°C. These temperatures are capable of causing bone necrosis at both the plug and interface.

Effect on Cartilage

Histologic examination showed that the layer of subchondral bone had been rendered avascular at the time of surgery by removal from the dog. The lacunae in the original subchondral bone were devoid of osteocytes. The interface between the subchondral bone and cement was composed of a very vascular layer of connective tissue, which was thicker than that reported by Charnley[1] for a similar interval (Figs. 2 and 3). No bone trabeculae extended to the cement boundary. This was the result of the technique used, in which the surface of the subchondral bone was made smooth with a dental burr and the cement placed directly against it instead of being packed into a confined space; the

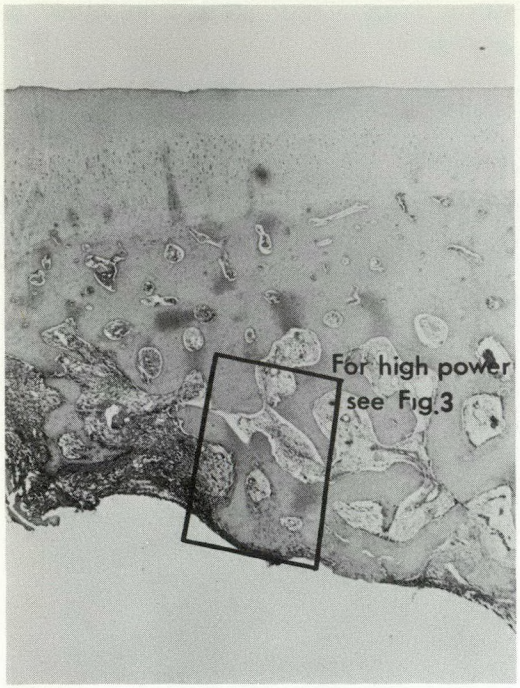

Fig. 2.—Area of articular cartilage and cement-bone junction (hematoxylin and eosin, x 25).

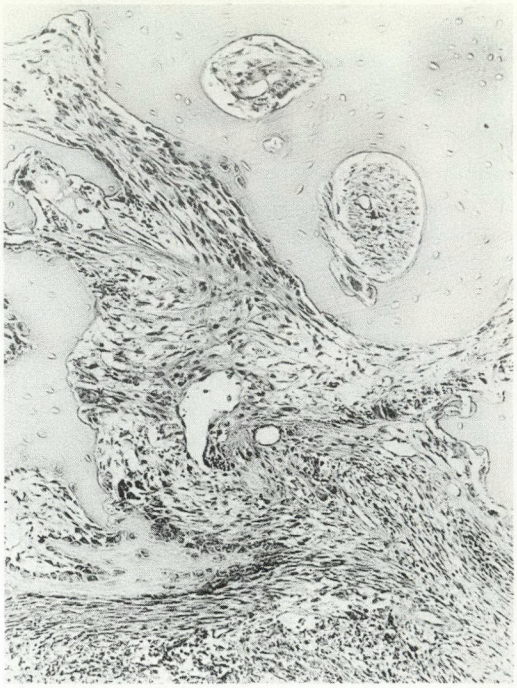

Fig. 4.—Junction of connective tissue and bone showing osteoclastic and osteoblastic activity (hematoxylin and eosin, x 50).

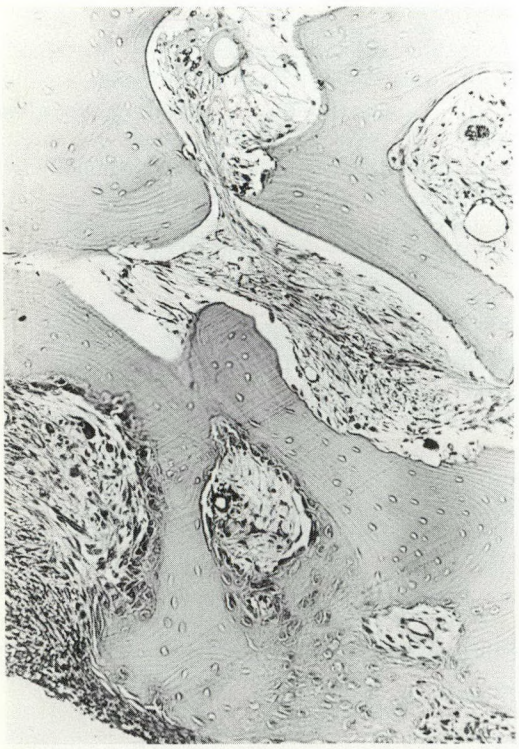

Fig. 3.—Detail of cement-bone junction from same section illustrated in Fig. 2 (hematoxylin and eosin, x 50).

Fig. 5.—Osteoblastic and osteoclastic activity in subchondral bone, with new bone deposition (methylene blue, x 50).

Fig. 6.—Normal articular cartilage (hematoxylin and eosin, x 50).

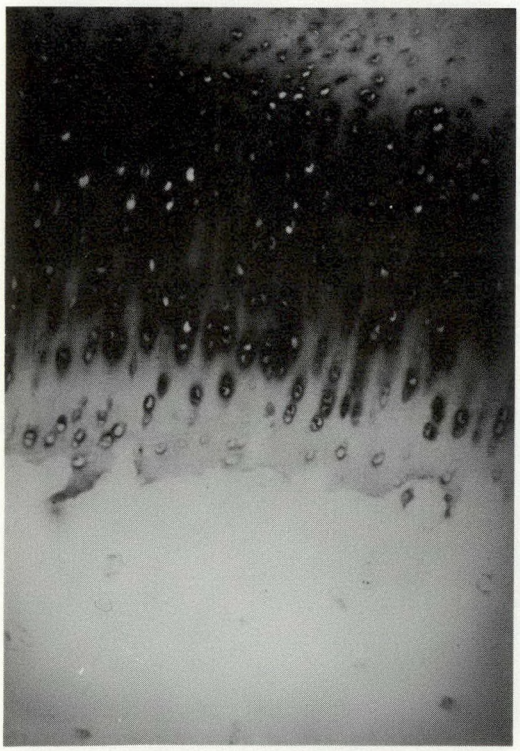

Fig. 7.—Normal metachromasia of chondrocytes (toluidine blue, x 10).

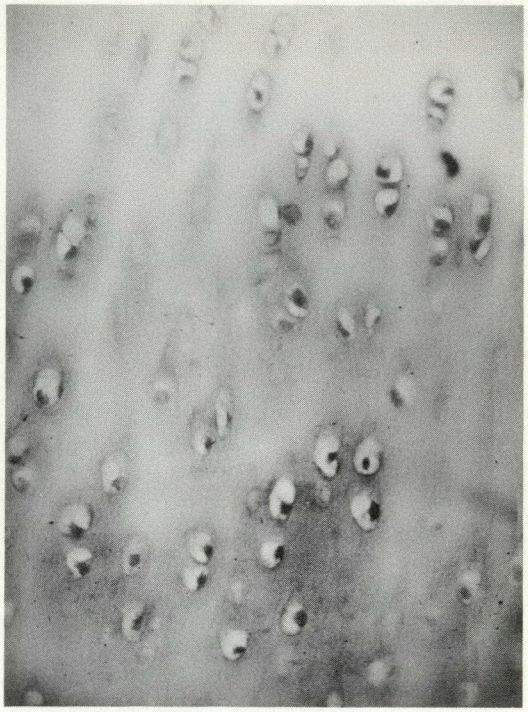

Fig. 8.—Normal metachromasia of chondrocytes (toluidine blue, x 50).

latter occurs during total hip replacement and results in cement being pushed between bone trabeculae.

At the junction of the connective tissue and subchondral bone, there was distinct osteoclastic and osteoblastic activity as the necrotic bone was resorbed and new bone deposited (Fig. 4). Osteoblastic activity could be seen throughout the entire thickness of the subchondral bone (Fig. 5).

The articular cartilage was normal (Fig. 6). There was no evidence of fissure formation, chondrocyte proliferation or vacuolation, or any alteration in the zone of calcification. Special stains for metachromasia showed the cartilage had normal staining characteristics (Figs. 7 and 8).

Conclusion

Temperatures recorded at the centre of the methylmethacrylate plug corresponded closely to those reported by Charnley and others. However, temperatures at the cement-bone junction, the area of greatest biologic significance, were slightly lower

(Continued on page 178)

when shock threatens the lung

Abstract visualization of lung tissue

Solu-Medrol

helps reduce pulmonary damage and increase survival rates

- preserves lysosome and cell membranes, thereby preventing the release of destructive lysosomal enzymes[3]
- preserves platelets thereby reducing the risk of intravascular coagulation[1]
- preserves leukocyte integrity thereby helping to maintain the pulmonary architecture[1]

The recovery of patients in shock is often complicated by a pattern of deteriorating pulmonary function. This pulmonary insufficiency progresses despite restoration of hæmodynamic balance and apparent stabilization of the acute episode.

Under conditions of prolonged shock, lack of oxygen at the cellular level causes alterations in the oxygen-carbon dioxide exchange mechanism. These changes in cell metabolism lead ultimately to interstitial œdema and perivascular hæmorrhage.[1] Polymorphonuclear leukocytes aggregate in the pulmonary capillaries and obstruct the pulmonary vascular bed. As these trapped cells break down, they release lysosomes, tiny subcellular particles containing proteolytic enzymes.[1] These enzymes attack their host cell and go on to damage or destroy other cells.[2] The resulting tissue damage may not readily repair itself even if the shock patient survives.

When administered in conjunction with standard therapeutic measures, Solu-Medrol exerts a protective effect on the lung and improves the patient's chance of survival.

Prescribing information on following page

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(Continued from page 175)

than those recorded by Homsy. Nevertheless, temperatures were still of an order high enough to cause bone necrosis.

There was no histologic evidence of any damage to articular cartilage caused by the close proximity of methylmethacrylate. Similar results were seen in all dogs. There was no evidence of sepsis in the subchondral bone, and no evidence of intra-articular reaction. There was osteoblastic activity adjacent to the cement, indicating that cells with osteogenic potential are not affected by the presence of the cement. Therefore, fractures fixed either by cement alone or using cement as an adjunct to metallic fixation can be expected to unite normally.

We acknowledge that these observations have not been substantiated over a long period, so we cannot comment on the possible long-term sequelae. However, because revascularization of the subchondral bone was noted at 6 weeks, the bone must be considered normal, and damage to the articular cartilage later seems unlikely.

We thank Dr. V. L. Fornasier for his expert interpretation of the histology. We also thank Mrs. I. Urquhart and M. Smith for their help in preparing the histologic sections, Miss D. Gedge for her patience in preparing the manuscript, and Miss M. Bliss and her staff for the preparation of the illustrations.

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PACEMAKER INFECTIONS: A 12-YEAR REVIEW*

GUY G. LEMIRE, MD, JEAN E. MORIN, MD and A. R. C. DOBELL, MD

Summary: In a 12-year period, 546 pacemaker-related operations were complicated by 23 infections (infection rate, 4.2%). Most of these infections were treated successfully, but two cases of infection were fatal. The most frequently encountered organism was Staphylococcus epidermidis. **In 14 cases, infection occurred despite the preoperative administration of cloxacillin to which the organism was sensitive in 13 of the cases. The skin flora constitute the most likely source of contamination. The ideal treatment consists of removal of all foreign material and replacement with a new pacing system by an alternative route.**

Résumé: Durant une période de 12 années, 546 interventions chirurgicales ont été pratiquées pour implanter ou changer les régulateurs du rhythme. Vingt-trois interventions ont été compliquées d'infection, pour un taux de 4.2%. La grande majorité de ces infections ont pu être traitées avec succès mais, dans deux cas, ont eu une issue fatale. Le germe pathogène le plus souvent rencontré était Staphylococcus epidermidis. **Dans 14 cas, l'infection est apparue malgré l'administration pré-opératoire de cloxacilline, antibiotique auquel le germe était sensible dans 13 des 14 cas. La flore cutanée représente la source la plus probable de contamination. Le traitement idéal consiste à enlever tout corps étranger et à le remplacer par un nouveau stimulateur cardiaque introduit par une autre voie.**

FOREIGN materials, such as synthetic grafts, heart valves, or pacemakers, that become infected present difficult problems. The purpose of this communication is to review our experience with infections of pacemakers with respect to the clinical features, the etiologic factors, the sequelae and our approach to the treatment of this type of infection.

PATIENTS AND SURGICAL PROCEDURES

During the 12-year period from 1961 to 1972 inclusive at the Royal Victoria Hospital, Montréal, 328 primary pacemakers were inserted and 218 pulse generators were changed—a total of 546 pacemaker procedures (Table I). Infection complicated 23 procedures in 20 patients (infection rate, 4.2%); 14 of these procedures were primary insertions and 9 were battery replacements.

ORGANISMS ISOLATED, SITES OF INFECTION, AND CLINICAL MANIFESTATIONS

Infection was confirmed by positive culture in 20 cases. The organisms isolated were *Staphylococcus epidermidis* (14 cases), *S. aureus* (2) and mixed (4). The sites from which the positive cultures were obtained included the pulse generator pocket (18), the electrode (8), the blood stream (3), the pericardium (1) and the pleura (1); in some cases, the same organism was cultured from more than one site. In the other three cases, obviously infected pacemakers failed to yield any organism on routine culture. Manifestations of infection included inflammation over the pulse generator pocket, erosion of the pulse generator through the skin, a draining sinus leading to the pacemaker electrode and bacteremia.

TREATMENT

The antimicrobial regimen at the time of the initial operation varied: 3 patients received no antimicrobials, 6 were given various antimicrobials after operation, and 14 were treated with cloxacillin in the preoperative and postoperative period for up to 7 days. In the period 1968 to 1972, cloxacillin was administered before and after operation in the majority of the 474 pacemaker-related operations; the 14 infections that occurred during this period all grew *S. epidermidis* that were sensitive to cloxacillin in every case but 1.

TABLE I.—PACEMAKER INFECTIONS 1961 TO 1972 INCLUSIVE

Pacemaker procedure	*Cases*	*Infections*	*%*
Transvenous insertion	267	10	3.7
Transthoracic insertion	61	4	6.6
Pulse generator change	218	9	4.1
Total	546	23	4.2

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Treatment of the 23 infections also varied according to the clinical situation. In general, the infected foreign bodies were removed, including the electrodes when possible. In two cases, closed-circuit irrigation of the infected pulse generator was attempted;[1] this was successful in one of the two cases.

Complications

Although early recognition prevented complications in most cases, septicemia occurred in three patients. Two case reports illustrate the range of complications that can occur.

Case Reports

Case 1.—A 58-year-old woman was admitted to the emergency room in cardiac standstill. A diagnosis of complete heart block was made and, after resuscitation, a transvenous pacemaker was inserted; no antimicrobials were given. She was discharged 5 days later. After 2 weeks, swelling around the pulse generator pocket was noted; 200 ml of serum were aspirated but culture failed to yield pathogenic bacteria. Then, 5 months later, an inflammatory reaction developed where the transvenous electrode crossed the clavicle. The lead and pulse generator were relocated; a small amount of serous fluid in the pocket was sterile on routine culture.

One year later, a draining sinus at the site of the previous inflammation over the clavicle was cultured and grew *S. epidermidis*. The sinus was exised and, because it did not appear to be in continuity with the electrode, the latter was left in place.

The patient was readmitted 7 months later because of fever and pain over the clavicle. The sinus was still present and *S. aureus* was cultured from the sinus tract and the blood stream. The infected pulse generator and transvenous electrode were removed, but the latter broke on traction, leaving a remnant in the right ventricle and atrium. Another permanent transvenous pacemaker was inserted during the same procedure. Ampicillin was given postoperatively until the 2nd postoperative day when cloxacillin, to which the bacteria were sensitive, was substituted. The patient's condition stabilized and improved until a skin reaction to cloxacillin was detected 2 weeks later. Cloxacillin was replaced by oxacillin but she reacted adversely to this, and acute anuria developed. Her condition deteriorated and she died 44 days after admission. This time, blood cultures grew *S. mitis* despite administration of lincomycin.

COMMENT.—We recognize that, despite her precarious condition, a thoracotomy should have been performed soon after the electrode had broken, to remove the remnant from her heart.

Case 2.—A 60-year-old man was found to have bacterial endocarditis secondary to bacteremia due to *S. epidermidis*. During a period of 20 months he had undergone several operative procedures related to electrode dislogment and infection of a pulse generator. Septic aortic valvulitis resulted in aortic insufficiency, for which emergency valve replacement was necessary. After a difficult postoperative course, the patient was sent home. He died suddenly 2 months later. An autopsy was not performed.

Discussion

Pacemaker infections, which are characterized by their apparently benign clinical course, usually present as a rather indolent, painful swelling of the pulse generator pocket, a draining sinus, or a skin ulceration through which the pulse generator may migrate. One facet of our study showed the predominance of *S. epidermidis* as the infective agent, which brings into question the pathogenicity of this organism. A well-known saprophyte of the skin, *S. epidermidis* should surely be considered a pathogen when it is found in the blood stream, in sinus tracts, or in infected pulse generator pockets. In most of our cases more than one positive culture was obtained, the clinical picture of infection was present and no other organism was cultured.

Certain patients react to the foreign material in pacemakers and, as a result, the skin becomes tight and thin around the pulse generator. This is particularly true in older, thin patients in whom the pulse generator has eroded through the skin. In these patients, it is impossible to determine whether the contamination with *S. epidermidis* occurs at the time of skin breakdown, at the initial operation or during the course of a transient bacteremia.

In our patients, the infections generally did not manifest themselves immediately after implantation; rather, they were detected months or years after the pacemaker

procedure. This would be in keeping with the low virulence of *S. epidermidis,* and it may be that the antimicrobial therapy in the perioperative period, as well as the patient's own defence mechanism, delayed the appearance of the florid infection.

The infection rate in this series of patients (4.2%) is high for clean surgical cases despite usual aseptic techniques. It is our impression that most wounds became infected at the time of operation, and the speed of propagation depended on the virulence of the organism, the antimicrobial regimen, and the host's defence mechanism.[2, 3]

In reviewing these cases, we attempted to identify factors that could predispose to infection. Procedures done in the operating room did not have a lower incidence of infection than those done in the cardiac catheterization laboratory or the x-ray department.

The role of antimicrobials certainly has not been clearly defined by this study. The general prophylactic use of antimicrobials remains controversial[4, 5] but in cardiac surgery numerous studies[6-8] show their value and usefulness. The ideal regimen, however, is in question. The choice of antimicrobials is important, and, in our institution, because of our bacteriologic data, a synthetic penicillin appeared to be the antimicrobial of choice. Our rationale for the use of cloxacillin was the effectiveness of this drug against our hospital's *S. aureus,* the organism that we initially wanted to combat. At present we no longer use antimicrobials prophylactically. We prepare the skin meticulously with green soap and iodine before making the incision and then, once the pacemaker has been inserted and before the wound is closed, we irrigate the wound with approximately 500 ml of normal saline solution containing bacitracin (50 U/ml) and polymyxin B (0.005%).

Serious complications of infection related to pacemakers are the direct result of bloodstream infection. Both patients who died and the patient who survived septicemia due to *S. epidermidis* were paced transvenously. This necessitates removal of all foreign material from the blood stream but it is not always easy. Intravascular pacemaker lead electrodes are covered by a tight sleeve of fibrous tissue that hugs the lead and its flanged tip, which is embedded in the right ventricle. Under the appropriate antimicrobial coverage, the foreign material must be extracted if the infection is to be cured. Unchecked bacteremia may result in metastatic spread of the infection, as in Case 2 in which bacterial endocarditis led to massive aortic insufficiency. Presented with the problem of removing an infected pacemaker, the physician should determine whether a pacemaker is still absolutely necessary. Extraction of the infected pacemaker and drainage would thus be the simplest form of treatment.

Must each infected pacemaker be removed entirely, not withstanding the extent of the infection or the route by which the pacemaker was inserted? Furman and associates[1] and others[9, 10] report the successful use of closed-circuit irrigation with the appropriate antimicrobial solution in the treatment of infection of the sternum. We attempted this twice. Although this represents a limited experience, the failure in one case, and a limited success in the other, were enough to discourage us from using this technique. The prolonged hospitalization, the limitation of the patients' activity especially the older patients, and the probable ineffectiveness in reaching the infected lead, all were factors that made the technique unattractive to us.

Our preferred technique in the case of an infected pulse generator when continued pacing is required is to divide the electrode some distance from the pulse generator and connect the cardiac end of the divided lead to an external pulse generator. The infected pacemaker can be removed and the pocket drained. Appropriate antimicrobials and local treatment of the infection are continued for several days. An entirely new pacemaker system is then inserted through an uninfected route, and the residual electrode is removed. Occasionally we have exposed epicardial electrodes where they entered the chest and, after applying moderate traction, have divided them leaving a short length of electrode attached to the heart's surface. Infected transvenous electrodes should be removed in their entirety. In one of our patients a thoracotomy was necessary for removal of an electrode from the right atrium.

Two deaths related directly to pacemaker infections underscore both the potential danger of all such infections, especially when the transvenous route is used, and the need for a definite plan in their treatment.

Conclusions and Recommendations

Infection of a pacemaker is potentially dangerous, especially in the case of pacemakers that have been inserted by the transvenous route. A definite plan for the treatment of pacemaker infections is necessary. We propose the following method of treatment:

(a) in bloodstream infections the pacemaker should be removed entirely and a new one inserted by another route;

(b) in localized infections, there is an option: (1) replace the entire pacemaker as in bloodstream infection; and (2) replace the pulse generator and splice to a "clean" lead remnant in a counterincision.

The transthoracic approach is now preferred to the transvenous route for most cases.

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POSTOPERATIVE INFECTIONS

Recent understanding of anaerobic infections, new laboratory aids to diagnosis of bacterial infection, and antibiotic sensitivity tests are topics considered by J. P. Burke (Abdominal Surgery *16: 288, 1974*). *Anaerobic infections have probably been overlooked or misdiagnosed in the past but there is no evidence that their frequency in increasing—though there is a possibility that the use of kanamycin and gentamicin has favoured the overgrowth of resistant strains of* Bacteroides sp. *and other anaerobes. But the major factors in diagnosing anaerobic infections are physician awareness and collection of appropriate specimens. Useful pointers are infection site (e.g. oropharyngeal area, gastrointestinal tract and female reproductive tract); thrombophlebitis; brain abscesses; a foul or putrid odour; absence of growth on routine culture or report of sterile pus from obviously infected material; and a culture report of a single organism from pus with various gram-positive and gram-negative bacterial forms. Effective treatment includes penicillin G (except for* B. fragilis) *or, for penetrating abdominal injuries, clindamycin in conjunction with kanamycin or gentamicin. Good surgical drainage is essential, along with application of hydrogen peroxide. And for the myonecrosis caused by* Clostridium sp., *hyperbaric oxygen.*

New laboratory aids include the nitroblue tetrazolium (NBT) and limulus tests and the gallium scan. The NBT test is useful in differentiating bacterial infection from nonbacterial disease with leukocytosis and fever but its early promise may not have been fulfilled. The limulus test is a sensitive assay for bacterial endotoxin and it may aid in the diagnosis of gram-negative bacteremia. But neither test may be as promising as ^{67}*Ga-citrate scanning, which permits visualization of abscesses (tumours also, so these must be excluded).*

Antibiotic sensitivity tests are now standardized. A uniform suspension of microorganism for the inoculum and measurement of diameters of zones of inhibition surrounding the antibiotic-containing discs are the main features of standardization. The potency of the discs and the zone diameter required to indicate susceptibility are unique for each antibiotic; there is correlation with serum antibiotic values. Despite this standardization, disc sensitivity is sometimes misleading even when performed in first class laboratories.

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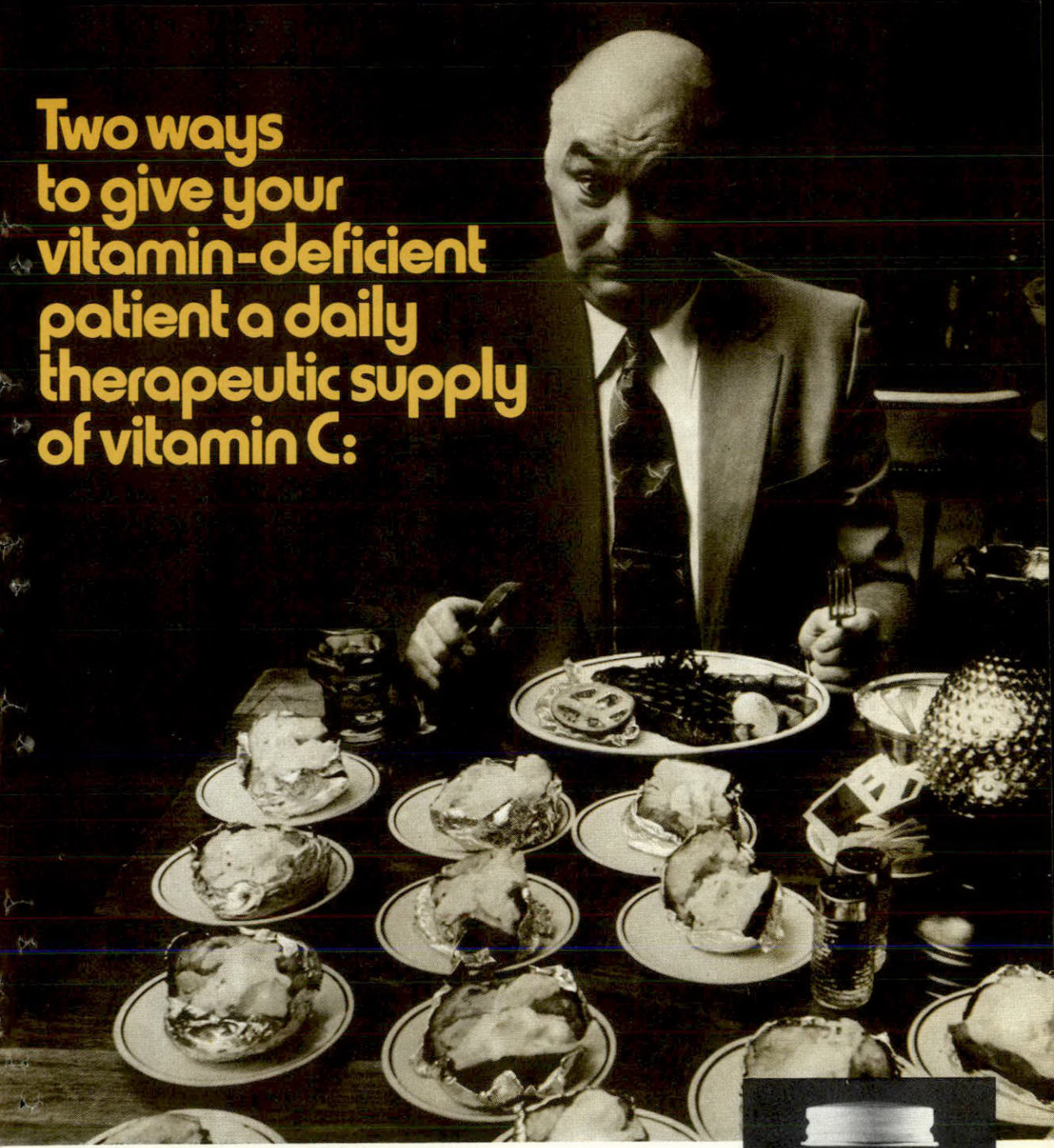

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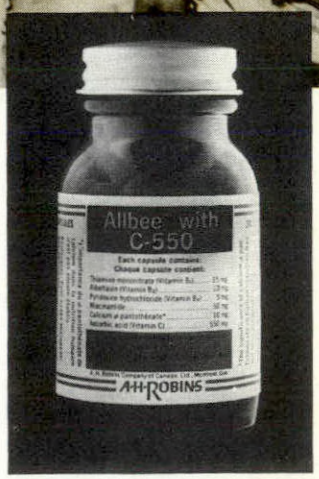

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GASTROCOLIC FISTULA COMPLICATING BENIGN GASTRIC ULCER: CASE REPORT AND REVIEW OF LITERATURE*

K. TAGUCHI, MD and J. G. BEAUDOIN, MD

Summary: A review of the literature and report of a case of benign gastrocolic fistula indicate that epigastric pain is the most frequent early symptom. Later, the predominant symptoms are diarrhea, weight loss and feculent vomiting. Patients suffering from rheumatoid arthritis and taking steroids appear to be particularly at risk of developing a gastrocolic fistula. Barium enema is the most reliable method of demonstrating the fistula. Preferred management is a one-stage gastrocolic resection and primary anastomosis.

Résumé: Après avoir passé en revue la littérature pertinente et étudié le rapport d'un cas de fistule gastrocolique, nous en sommes venus à la conclusion que le symptôme précoce le plus fréquent est une douleur épigastrique. Plus tard, la diarrhée, la perte de poids et des vomissements fécaloïdes deviennent les symptômes prédominants. Le risque d'apparition d'une fistule gastrocolique est particulièrement élevé chez les malades souffrant de polyarthrite rhumatoïde qui sont traités par les corticoïdes. Le moyen diagnostique le plus sûr pour confirmer la fistule est le lavement baryté. Le traitement préférentiel est la résection gastrocolique en un temps et l'anastomose primaire.

GASTROCOLIC fistula is a rare complication of benign gastric ulcer. To date 56 cases have been reported in the English literature.[1-18] Many of those recorded were reviewed in this journal by Sterns and Bird;[18] this communication presents an additional case report.

CASE REPORT

In September 1973, a 44-year-old man attended the emergency department of the Royal Victoria Hospital, Montréal because of a gastrointestinal hemorrhage. The patient had suffered from rheumatoid arthritis for 10 years and at the time of his admission the condition was controlled by methylprednisolone, 6 mg, and acetylsalicylic acid (ASA), 3.6 g, daily. He denied any history of ulcer disease. Fever and left lower abdominal pain 3 months before admission were followed by foul eructations and an increased frequency of defecation. On the morning of his admission he was awakened by an urge to move his bowels; hematemesis and melena developed before he was admitted to hospital.

He appeared extremely anxious. Cushingoid features were evident. Abdominal examination revealed neither tenderness nor a palpable mass The hemoglobin concentration was 10.7 g/dl and the leukocyte count was 10 000/ mm^3.

Gastric lavage with iced saline through a Levin tube quickly stopped the hemorrhage. Gastroscopy revealed a benign chronic gastric ulcer from which, at the time, there was no active hemorrhage; radiography of the upper gastrointestinal tract showed a spontaneous gastrocolic fistula (Fig. 1). A hemigastrectomy with Billroth I anastomosis was performed 5 days after admission. The colonic fistula was dissected free, the scar tissue was excised and the colon was closed in two layers. Recovery was uneventful, and the patient was discharged on the 10th postoperative day.

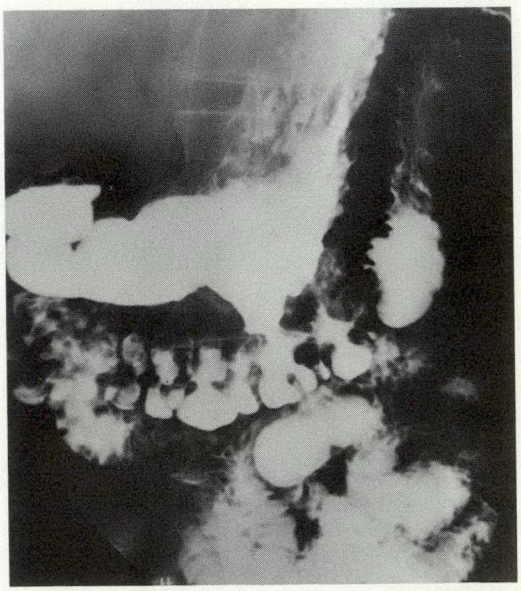

Fig. 1.—Spontaneous gastrocolic fistula.

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Reprint requests to: Dr. K. Taguchi, department of surgery, DIII, Kingston General Hospital, Kingston, Ont. K7L 2V7.

Discussion

Cancer of the stomach and of the colon are the most common, nonsurgical causes of gastrocolic fistula.[19] Marshall and Knud-Hansen[20] reported 11 such cases in a review of more than 4700 cases of cancer of the stomach or colon (incidence, 0.23%). In a series of 29 cases of malignant gastrocolic fistula reported from the Mayo Clinic, 17 were due to cancer of the colon;[21] at the same centre only a single case of gastrocolic fistula from benign gastric ulcer has been observed. Nevertheless, peptic ulcer disease is the second most common non-iatrogenic cause of gastrocolic fistula. Other rare causes are tuberculosis, subphrenic abscess, trauma, ulcerative colitis,[22] radiation,[23] pancreatic cancer,[23] carcinoid tumour,[24] and lymphoma.[19, 20]

Usually the history of patients who have a benign gastrocolic fistula can be separated into two phases. The first is related to the gastric ulcer disease when the patient complains of epigastric pain, burning, belching and anorexia. The clinical picture changes abruptly as the ulcer perforates into the colon: the patient now complains of diarrhea, weight loss and feculent vomiting. The diagnosis of a gastrocolic fistula can often be made on the basis of such a history. Feculent vomiting in the absence of obstruction, or the passage of undigested food per rectum is virtually pathognomonic of a gastrocolic fistula. The diarrhea noted by many of these patients is due to fecal reflux into the stomach. This was shown by Pfeiffer[25,26] and Jew, Levowitz and Fisher[27] who demonstrated that a proximal colostomy could completely control the diarrhea in these patients and that fecal contamination of the stomach and small intestine resulted in hyperperistalsis and diarrhea.

Table I indicates the frequency of symptoms in the 33 patients (including the present case) with benign gastrocolic fistula whose cases have been reported since 1920. Of these 33 patients 9 were taking steroids; 6 were treated with steroids alone and 3 with ASA as well—a striking finding when one remembers that steroids have been available for only about 20 years. Steroids have long been thought to be ulcerogenic.[28] Recent investigation in man, however, indicates that steroids given for either short or long periods do not increase the basal secretion of acid from the stomach.[29-31] Furthermore, no significant difference in peptic ulcer formation was found between patients receiving steroids and controls (incidence, 2.4 and 2.3%).[32] Thus, it would appear that steroids are not ulcerogenic.

Seven of the nine patients taking steroids suffered from rheumatoid arthritis. The reported incidence of peptic ulcer in the general population in an annual survey is 1 to 3%[33] and two to four times higher in patients with rheumatoid arthritis.[34, 35] Although much of this increased susceptibility may be attributed to the use of ASA, even patients with rheumatoid arthritis who do not use ASA have a greater incidence of dyspepsia (40%) and peptic ulcer (13%).[36] The addition of steroids to the therapy appears to augment the tendency towards peptic ulcer formation. In a cumulative study of 1713 patients on long-term steroids for various conditions, the incidence of peptic ulcer was 3.1% compared with 10.4% in 1837 patients taking steroids for rheumatoid arthritis.[37] Perhaps a truer incidence can be determined from the prospective study done by Kammerer, Freiberger and Rivelis.[30] Among 117 patients receiving steroids for rheumatoid arthritis who, regardless of symptoms, were given a barium meal, peptic ulcer disease was radiologically evident in 36 (31%); but among 33 patients with rheumatoid arthritis not receiving steroids such evidence was noted in only 3 (9%). In a control group of patients with arthritis other than rheumatoid, who were not receiving steroids, only 2 of 37 (5%) showed radiologic evidence of ulcer. It appears that steroids given to patients with rheumatoid arthritis greatly increase the incidence of peptic ulceration.

TABLE I.—Principal Symptoms in 33 Patients with Gastrocolic Fistula from Benign Gastric Ulcer

Symptom	*No. of patients (and %)*
Abdominal and epigastric pain	22 (67)
Diarrhea	20 (61)
Weight loss	21 (64)
Vomiting	17 (51)
Hematemesis and/or melena	11 (33)

Steroids have been shown to retard the healing of acute gastric ulcers in dogs[38] and to inhibit the incorporation of radioactive sulfur into the mucus-secreting glandular cells of the stomach.[39] This interference with the healing process may explain the frequent association of gastrocolic fistula in patients with rheumatoid arthritis who are receiving steroids.

Thoeny, Hodgson and Scudamore[40] claimed that barium enema was the most reliable means of diagnosing gastrocolic fistula. They examined 41 patients by barium enema or barium meal, or both, and demonstrated the fistula in all 30 patients who were given a barium enema but in only 9 of 35 patients given a barium meal. In reviewing 33 cases recorded in the literature in which radiologic investigations had been carried out, the findings were essentially in agreement with those of Thoeny, Hodgson and Scudamore; the discrepancy, however, was not nearly as great as suggested by the study of Thoeny, Hodgson and Scudamore. In all 19 patients who were given a barium enema, the fistula was demonstrated by the enema, but the fistula was demonstrated in only 16 of 21 patients who had a barium meal. In the five patients in whom a barium meal failed to reveal the fistula, a barium enema was successful.

Management of gastrocolic fistula has generally been by a one-stage resection of the stomach and colon and primary anastomosis. With respect to the procedures performed on the 33 patients whose cases we reviewed, 26 were one-stage procedures, 5 were staged procedures, 1 was a laparotomy only and the details of the other were not described. With respect to mortality, one patient who underwent a staged procedure died, both of those in whom gastric and colonic fistulas were closed without resection died, and the patient who had a laparotomy only died.

Complications have been few. There is only a single report of a colonic fistula which healed quickly after resection.

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EXPERIENCE WITH 300 LIVING RELATED KIDNEY DONORS

Renal transplantation is an everyday occurrence, and it is more than 20 years ago since Hume and his colleagues (at the Peter Bent Brigham Hospital) in Boston introduced the procedure by using a cadaver kidney. Two years after this, Brigham surgeons became the first to transplant a kidney from a living related donor, the first of some 350 kidneys to date that have been transplanted in this one institution. Bennett and Harrison (Surg Gynecol Obstet *139: 894, 1974*) *now describe the Brigham's experience, almost exactly 20 years later, with the first 300 living related donors.*

As the authors note, "Certain morbidity and mortality statistics are involved when a patient undergoes an extensive surgical procedure," and the statistics are of especial interest when such a patient is generally healthy. Of this group of 300 donors, 251 were healthy and 49 had physical abnormalities that were not serious enough to contraindicate surgery. The overall complication rate, however, was 28.6%. There were 16 major complications among 13 donors (wound infection in 5, pneumonia in 5, acute renal failure secondary to sepsis in 1, wound hernia in 1, psychosis in 1, upper gastrointestinal hemorrhage in 1, serum hepatitis in 1 and postoperative hepatitis—which caused the only death in the series—in 1 patient). There were 102 minor complications among 28 donors; the majority comprised pulmonary and urinary problems. The 49 donors with miscellaneous diseases included 12 with chronic pulmonary disease, 11 with hypertension, 9 with recurrent cystitis, 6 with obesity, 4 with diabetes mellitus, 3 with inactive pyelonephritis, 2 with inactive tuberculosis, 1 with recurrent vesical papilloma, and 1 with Parkinson's disease. An interesting finding was postoperative psychiatric disorder in 20 patients.

The mortality among the 350 donors who have undergone nephrectomy to date stands at 0.29%—a remarkable rate considering the seriousness of the procedure and the age range of the patients, which was from 12 to 80 years. Bennett and Harrison report the interesting item that, across the world, five living related donors have died from causes related to the procedure.

Perhaps unexpected was the incidence of psychiatric problems. Evidently the donation of a kidney, even to a close relative, engenders emotional strain within a family. The authors did note, however, that a number of donors said that information from other donors would have been helpful. Thus, though renal transplantation is now rightly an accepted surgical procedure, it is one that is by no means straightforward. The findings reported by Bennett and Harrison will therefore be of much interest to all physicians and surgeons.

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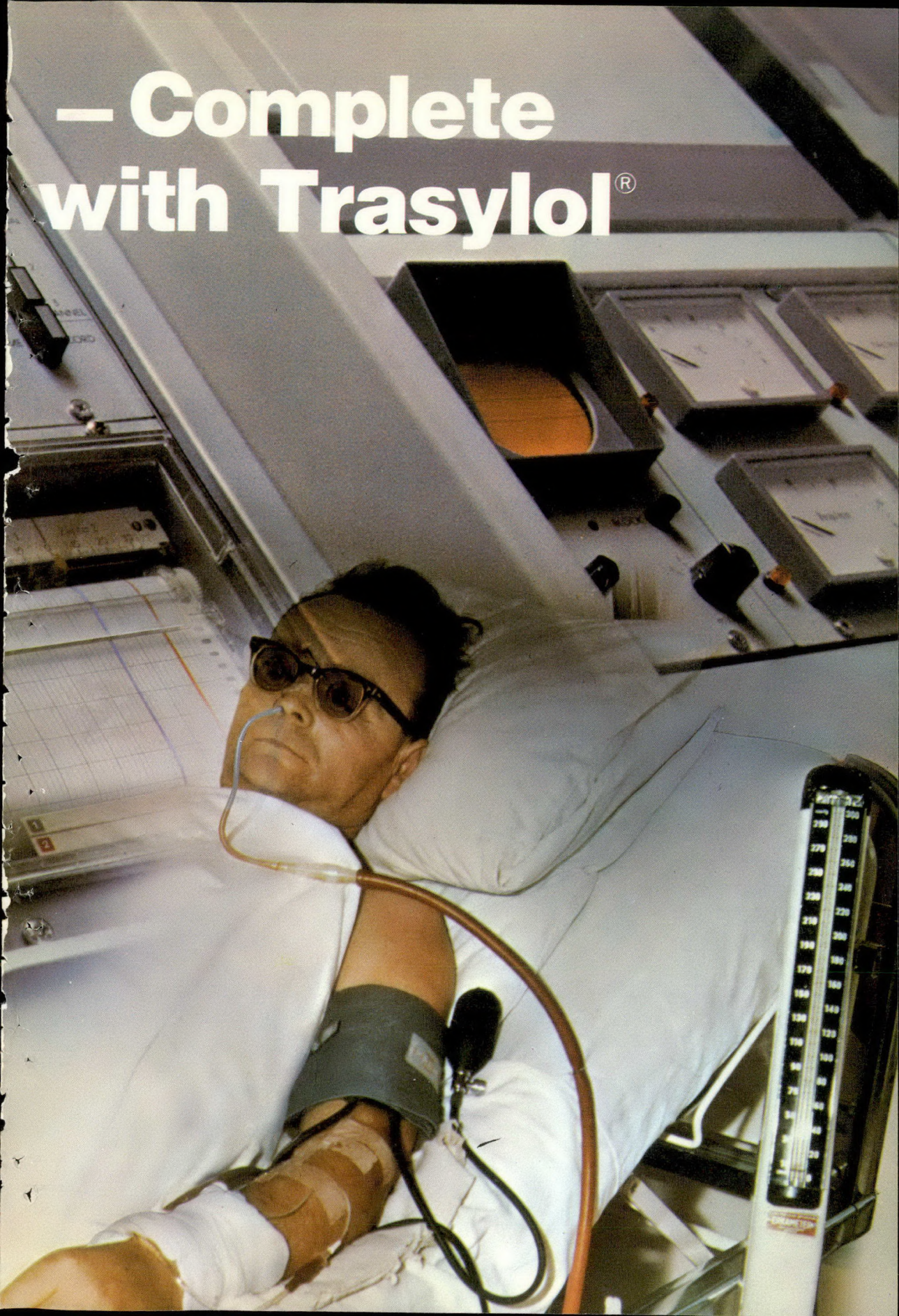
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LA CHOLÉCYSTITE EMPHYSÉMATEUSE: PRÉSENTATION DE DEUX CAS CLINIQUES

E. SAMSON, MD, FRCS[C], FACS,* A. KIBRITE, MD, FRCS[C], et J. P. ROY, MD‡

Résumé: Nous profitons de la présentation de deux cas de cholécystite emphysémateuse traités dans notre institution, pour faire une revision de la littérature à ce sujet. Les différents aspects étiologiques, symptomatiques et pathologiques sont exposés, et nous terminons en comparant les résultats de l'étude clinique de nos deux cas à celle exposée par les différents auteurs.

Summary: Emphysematous cholecystitis is relatively rare: in 1971 the cumulative total of cases reported in the world literature was 115. Two cases seen in the period 1967 to 1972 can be added. The features of these two cases, and those described in the literature support the view that emphysematous cholecystitis results from a primary obliterative endarteritis and a secondary proliferation of microorganisms.

La cholécystite emphysémateuse est une pathologie rare, dont le diagnostic fut facilité par l'avènement de la radiologie. Cette maladie semble avoir une étiologie différente[1] de celle de la cholécystite aiguë habituelle; d'ailleurs l'étude de la centaine de cas existants[1, 2] dans la littérature a permis à plusieurs auteurs[1-6] de trouver des faits symptomatiques communs permettant de différencier cette maladie de la cholécystite aiguë rencontrée habituellement et de la traiter dans un chapitre à part au sein de la pathologie vésiculaire. L'étude de nos deux cas nous a permis d'être en faveur de la théorie de May et Strong.[1] Cependant pour l'affirmer complètement, il est important de faire une étude sur un plus grand nombre de cas.

Histoire de Cas

Cas no 1.—Le 6 janvier 1967, un homme, âgé de 71 ans, présente une douleur abdominale à début assez subite, localisée à l'hypochondre droit avec irradiation para-ombilicale droite et vers la fosse iliaque droite. Cette douleur était accompagnée de trois à quatre vomissements bilieux et d'une température à 38.8°C. Le patient consulte un médecin qui lui donne de la pénicilline en injection intramusculaire. Le 8 janvier 1967, le patient se présente à l'urgence, avec une douleur à l'hypochondre droit et à la région para-ombilicale droite, température 38.3°C. Diabète mis en évidence depuis 1 mois.

L'examen physique montre un patient avec un état général satisfaisant, à l'auscultation pulmonaire une diminution du murmure vésiculaire surtout à la base droite, avec diminution de l'amplitude pulmonaire à ce niveau. A la palpation de l'abdomen, douleur maximum à l'hypochondre droit et sensation d'un plastron à ce niveau, péristaltisme faible. Le restant de l'abdomen est négatif. Les examens de laboratoire montrent: des globules blancs à 13 600/mm^3, la glycémie à 182 mg/dl avec une glycosurie à 2.5 g/l. La radio-pulmonaire montre une atélectasie linéaire dans les deux poumons, avec léger comblement du cul de sac diaphragmatique. Une radiographie simple de l'abdomen donne le diagnostic de cholécystite emphysémateuse (Figs. 1 et 2).

Il fut opéré le 10 janvier. A l'opératiton, on note que la vésicule biliaire (Fig. 1) était très distendue, sa paroi était nécrosée. Elle contenait du gaz et des calculs.

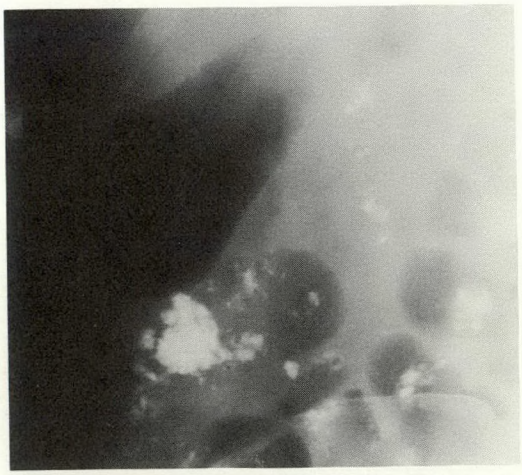

Fig. 1.—Cas no 1. Radiographie simple de l'abdomen, qui montre une vésicule biliaire pleine d'air.

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‡Interne, L'Hôtel-Dieu de Québec.

Les demandes de tirés-à-part doivent être adressées au: E. Samson, MD, département de chirurgie, l'Hôtel-Dieu de Québec, 11 Côte du Palais, Québec, PQ. G1R 2J6.

Aucune fistule avec le tractus gastro-intestinal n'a été identifiée. La cholangiographie par le cystique était normale. Une culture de la bile est revenue négative.

Cas no 2.—Un homme, âgé de 49 ans, référé d'un autre hôpital le 26 juillet 1972, avec le diagnostic de pancréatite aiguë. A son admission dans l'autre hôpital, il présentait une douleur à l'épigastre et à l'hypochondre droit, avec irradiation dans le dos. Ses examens de laboratoire ont montré: une leukocytose à 25 000/mm^3, une amylasémie à 2501 unités Somogyi /100 ml.

La radiographie simple de l'abdomen montrait un iléus paralytique. Il fut traité médicalement sans résultat et fut alors transféré à L'Hôtel-Dieu de Québec.

A son arrivée à L'Hôtel-Dieu de Québec, il était souffrant, d'apparence toxique, température à 37.2°C, la tension artérielle à 120/75 mm Hg et il présentait les signes d'abdomen aigu avec douleur très importante à l'épigastre et à l'hypochondre droit, avec irradiation aux deux épaules, et à la palpation on a l'impression d'une masse mal définie à l'hypochondre droit. L'interrogatoire met encore en évidence la prise de corticoïde depuis 1 an.

Les examens de laboratoire ont montré une lenkocytose à 11 750/mm^3, une amylasémie à 697 U/ml et une bilirubine totale à 1.97 mg/dl. La radiographie simple de l'abdomen montre une vésicule pleine d'air (Fig. 3).

A l'opération pratiquée le 29 juillet 1972, on note la présence d'une réaction inflammatoire très importante au niveau de la région pancréatico-biliaire. La vésicule biliaire était très distendue, oedémateuse et en voie de nécrose. On note la présence de gaz et de calculs à l'intérieur. Aucune fistule avec le tractus gastro-intestinal n'a été mise en évidence. Il existe une pancréatite aiguë nécrosante avec abcès.

Un prélèvement de la paroi vésiculaire a été fait pour la bactériologie, aucun résultat ne nous est parvenu à cause d'une erreur technique.

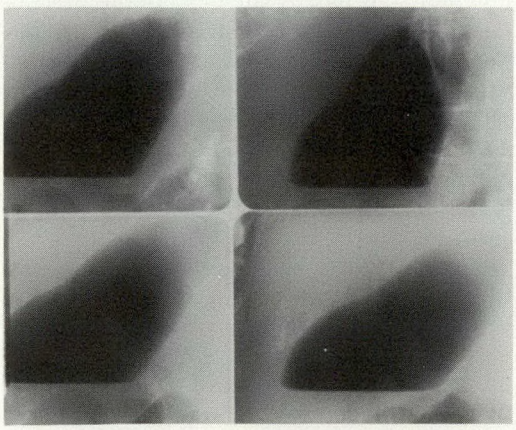

Fig. 2.—Cas no 2. Radiographie simple de l'abdomen en position debout centrée sur la région vésiculaire. On voit la vésicule biliaire remplie d'air avec un niveau liquidien.

La cholécystite emphysémateuse est une affection qui se caractérise par trois notions bien précises: sa rareté, son diagnostic qui est surtout radiologique et son cadre pathologique de plus en plus individualisé au sein de la pathologie vésiculaire.

Historique

Depuis la fin du 19e siècle et le début du 20e, plusieurs auteurs ont rapporté des cas de cholécystite emphysémateuse. Les cas présentés étaient soit des découvertes d'autopsie, soit des découvertes au cours d'une chirurgie abdominale.[1, 7-10] Ces chirurgiens ont décrit, au cours des cholécystectomies pour cholécystite aiguë, des vésicules biliaires pleines de gaz et parfois même avec une paroi crépitante signant un emphysème à ce niveau. La première fois que le diagnostic fut posé préopératoirement, ce fut en 1931 par Hegner[1, 11] grâce à la radiologie. Depuis les publications se multiplièrent, McCorkle et Fong[1, 12] en 1942 rapportèrent trois cas, dont le premier patient décéda

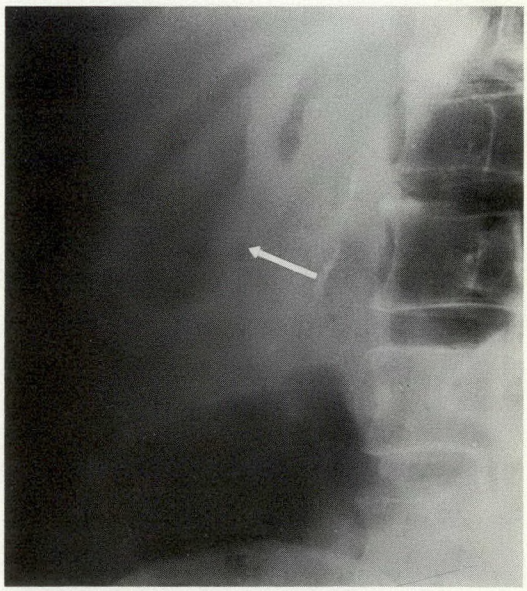

Fig. 3.—Cas no 2. Radiographie simple de l'abdomen, qui montre une vésicule biliaire pleine d'air (flèche).

d'une infection gazeuse fulminante de la paroi abdominale, les cultures ont montré du *Clostridium perfringens* et *Escherichia coli*.[1]

D'autres cas ont été rapportés par Jemerin,[1, 13] et Wilson.[1, 14] Heifetz et Wyloge[15] en 1955 reproduisirent expérimentalement l'aspect radiologique. Rosoff et Meyers[3] présentèrent 10 cas. Et en 1966, encore, Sarmiento[2] présenta un rapport portant sur 105 cas réunis à partir de la littérature mondiale. Enfin en 1971, May et Strong[1] présentèrent une étude basée sur la revision de 115 cas de la littérature mondiale et proposèrent une nouvelle théorie physiopathologique.

Cliniquement, la cholécystite emphysémateuse s'annonce comme n'importe quelle cholécystite aiguë par une douleur sous-costale droite avec irradiation dans le dos ou à l'épaule droite; ses sines cliniques sont identiques. L'examen physique, en plus des signes trouvés habituellement, montre souvent la présence d'une masse palpable.[1] L'ictère est noté dans 23.8% des cas.[2] En 1958 Wilson[1, 14] rapporte que ses patients semblent plus toxiques et plus malades que la clinique peut suggérer.[1] Au point de vue âge et sexe: la catégorie d'âge la plus fréquemment atteinte se trouve entre 50 et 70 ans; cependant dans les cas rapportés, on trouve des variations allant de 27 à 88 ans. A l'encontre de la cholécystite aiguë, l'incidence de cette maladie est trois à quatre fois plus élevée chez les hommes que chez les femmes (73.3% hommes pour 26.7% femmes).[2]

Deux notions importantes ont été rapportées par plusieurs auteurs: (1) 25 à 30% des cas avaient un diabète gras diagnostique[1, 3] et (2) la cholélithiase existe dans 50% des cas de la cholécystite emphysémateuse tandis qu'elle existe dans 85 à 95% des cas de la cholécystite aiguë.[16]

Le laboratoire montre une leukocytose plus augmentée dans la cholécystite emphysémateuse (dans 91.6% des cas les globules blancs > 10 000/mm^3 tandis que le pourcentage est de 67% pour la cholécystite aiguë.[4])

Radiologie

Le diagnostic de cette affection est radiologique et se base sur la présence de gaz dans la vésicule biliaire, dans sa paroi, ou dans le tissu périvésiculaire.

L'aspect d'un halo de gaz concentrique assez régulier prenant la forme d'un anneau dans la paroi vésiculaire est un diagnostic pathognomonique.[3] Cette distribution peut être parfois irrégulière et peut même se trouver dans le tissu périvésiculaire; cet aspect est encore très suggestif du diagnostic de cholécystite emphysémateuse. Quand le gaz est dans la lumière vésiculaire, le diagnostic différentiel se pose avec: (1) une fistule cholécysto-duodénale ou une fistule cholécysto-gastrique. Un repas baryté permettra de trancher le diagnostic,[3] (2) gaz dans un abcès du quadrant supérieur droit, (3) incompétence du sphincter d'Oddi. (La cholangiographie intra-veineuse permet, dans ces deux derniers cas, de préciser le diagnostic.)

Les études expérimentales de Heifetz et Wyloge en 1955[15] ont montré que, une fois la vésicule biliaire remplie de gaz, une rupture se fait dans la muqueuse près du canal cystique où la couche musculaire est déficiente, permettant ainsi au gaz de fuser dans la couche périmusculaire jusqu'à sa rupture vers l'extérieur (des radiographies prises durant ces expériences ont montré un aspect identique à la cholécystite emphysémateuse).

Etiopathogénie

Les différences étiologiques existantes entre la cholécystite aiguë et la cholécystite emphysémateuse rendent les explications pathologiques ambiguës. Ces différences étiologiques sont basées sur des notions statistiques à savoir: Affection deux à trois fois plus fréquente chez les hommes que chez les femmes.[1, 2] Approximativement 25 fois plus fréquente chez les diabétiques;[1, 2] 50% avaient des cholélithiases associées, 8.9% cholédocholithiase[1, 2, 6] (tandis que la cholécystite aiguë est associée à une cholélithiase dans 85 à 95% des cas).

Au point de vue bactériologique, Sarmiento[2] a noté dans son étude que les cultures de la bile ou de la paroi étaient positives dans 54.3% des cholécystites emphysémateuses; un organisme clostridial a été trouvé dans 24.8%, le *Clostridium perfringens* dans 20.9%, l'*Escherichia coli* dans 17.1%. Dans le restant des cas, on a noté la présence du streptocoque et du staphylocoque anaérobi,

de l'entérocoque et du protéus. Rosoff et Meyers[3] dans leur série de 10 cas étudiés notèrent 7 cas de culture positive de la paroi et chaque fois des bactéries capables de donner du gaz ont été identifiées.

Gordon-Taylor et Whitby[17] en examinant au point de vue bactériologique 50 vésicules biliaires ont trouvé le *Clostridium perfringens* dans 18% des cas et l'*Escherichia coli* dans 30% des cas.

A la fin de cette étude bactériologique, il est à noter que la bile peut rester stérile malgré des dommages parfois sérieux à la vésicule biliaire. Andrews et Henry[3, 18] et d'autres auteurs ont démontré que la bile reste bactéricide si la concentration des acides biliaires est 70% de la normale; cependant les changements inflammatoires dans la vésicule biliaire peuvent amener une réduction de cette concentration qui peut être le facteur permettant alors aux bactéries de se multiplier.

En revisant ces notions, il est difficile d'accepter comme théorie étiopathogénique de la cholécystite emphysémateuse, la même que celle de la cholécystite aiguë (Fig. 4); c'est d'ailleurs pourquoi, que May et Strong[1] ont procédé à l'étude histopathologique de leur trois cas de cholécystite emphysémateuse publiés. Ces deux auteurs ont noté dans les sections histologiques examinées, que les vaisseaux des parois de ces vésicules sont considérablement rétrécis par du tissu fibreux et que certaines lumières étaient complètement fermées. Dans d'autres coupes, les vaisseaux apparaissaient partiellement recanalisés. Afin de pouvoir faire une étude comparative May et Strong ont étudié histologiquement les parois de 60 vésicules biliaires enlevées pour cholécystite récidivante. Ils ont noté alors une endartérite oblitérante qui affectait quelques-uns seulement des vaisseaux sanguins, mais aucun de ces vaisseaux n'a été complètement fermé. Ces trouvailles ont amené les deux auteurs à suggérer que la cholécystite emphysémateuse peut être le résultat d'une occlusion vasculaire primaire de l'artère cystite ou de ses branches, qui aboutit à une ischémie au niveau de la vésicule biliaire qui à son tour fournirait les conditions nécessaires pour la multiplication des micro-organismes qui peuvent exister dans la bile ou la paroi vésiculaire (Fig. 4). Toujours selon ces auteurs, leur théorie pourrait expliquer le début aigu de la douleur, et l'incidence augmentée de la maladie chez les hommes et chez les diabétiques, tous deux plus affectés par les maladies vasculaires.

Discussion

Si nous comparons nos deux cas à ceux rapportés par les différents auteurs, nous notons beaucoup de similitude dans la clinique: Hommes, début subit, diabète etc. Au point de vue histopathologique, l'image décrite par May et Strong[1] existe dans le premier cas. Ce fait, de même que la revision de la littérature, nous permettent de favoriser la théorie de May et Strong. Une étude sur un plus grand nombre de cas est importante cependant pour accepter ou refuter cette théorie.

Au point de vue thérapeutique, certains auteurs trouvent que la cholécystite emphysémateuse ne nécessite pas toujours un traitement chirurgical d'urgence, et qu'elle répond très bien à l'antibiothérapie.[5]

Cependant, il ne faut pas oublier que la mortalité en cas de perforation est de 40 à 60%.[2] Ce qui nous amène à prendre une attitude aggressive envers cette affection, et chaque fois que nous diagnostiquons une cholécystite emphysémateuse, nous intervenons sous couvert d'antibiotiques, sans oublier cependant de bien évaluer nos patients.

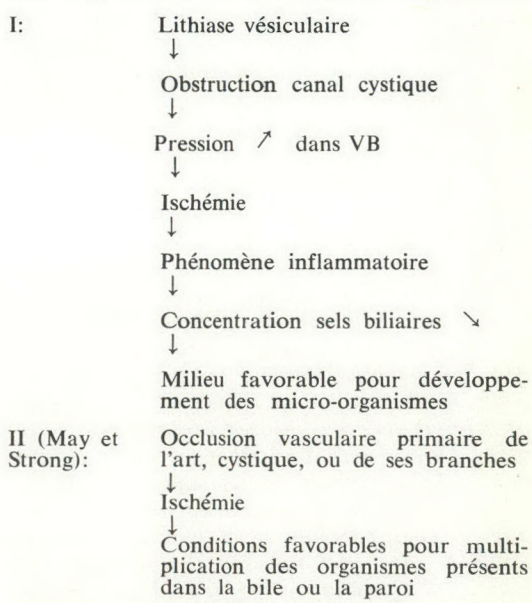

Fig. 4.—Etiologie des cholécystites emphysémateuses: deux hypothèses.

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SURGEONS' HAND INJURIES

The hand is as vital to the surgeon as it is to the pianist, the painter or the horologist. All of these dexterous artists face disability as a result of serious hand injury, which is bad enough, but injured surgeons may even face the risk of death. In an account entitled "Some Surgeons and their Hand Injuries" (Practitioner *213: 717, 1974*), *Bryan Williams describes hand injuries sustained by famous surgeons. The list of such surgeons is impressive; but every surgeon must subliminally if not consciously be aware of the vulnerability of this part of the body during professional work, quite apart from times of leisure.*

Semmelweiss based his ideas on the route of infection in puerperal fever on the course of fatal septicemia in his colleague Kolletschka, who had injured a finger during an autopsy. But Semmelweiss later suffered a similar tragedy, for he died from the effects of infection of a finger that was injured while he was operating. Others who died from infection secondary to hand injuries include the gynecologists Pfannenstiel, Porro and Schuchardt and the pioneer chest surgeon, H. P. Nelson. Williams, however, does not mention the surgeon with whom all Canadian surgeons will be familiar: Norman Bethune.

Many other surgeons have escaped death but have been disabled from hand injuries sustained during their work. Hamilton Bailey pinched his left index finger while operating on a patient who had peritonitis; a colleague amputated his finger, which had become stiff, but Bailey found that the smaller hand gave him greater dexterity. Others who overcame disability were William Blair Bell, the obstetrician and gynecologist, John Bland-Sutton, the surgeon and pathologist, and the chest surgeon Hugh Morriston Davies, who learned to operate with his left hand, devising instruments to hook onto his crippled right hand.

Surgeons, like other health professionals, have always risked contracting infection during their work. Conditions were worse in the pre-glove, preantibiotic era; and infections such as active syphilis were rampant in years gone by. At least one surgeon is known to have noticed, with horror, a primary syphilitic infection on a finger. Today, too, disposable equipment, "break-easy" glass tubes, and plastic envelopes make the surgeon's life safer. But even today surgeons must continue to be aware of dangers; for example, the risk of hepatitis is something that must be faced by anyone who handles donor blood or who works in dialysis units.

Williams' account is short, direct and essential reading for all concerned with hospital safety.

BOOK REVIEWS

ADVANCES IN CARDIOVASCULAR SURGERY. Edited by John W. Kirklin. Clinical Cardiology Monographs. 279 pp. Illust. Grune & Stratton, Inc., New York; Longman Canada Limited, Toronto, 1973. $18.00.

The appearance of "Advances in Cardiovascular Surgery", edited by John W. Kirklin, must be considered a major event in the medical publishing world. The selection of topics, as well as of contributors, is authoritative and could only have been achieved by a person with a deep knowledge and vast experience in his specialty.

The first half of the book deals with corrective surgery of congenital malformations of the heart and covers late results, complex congenital malformations, and primary definitive intracardiac procedures. In essence, this section is concerned with pediatric open-heart surgery and therefore has limited appeal, but candidates for the fellowship examination in cardiovascular surgery will find it most enlightening and helpful in supplementing their basic reading. Late results will be of interest to all cardiac surgeons as well as to cardiologists. In chapters dealing with definitive intracardiac operations, the authors contrast the risks and mortalities of staged procedures with the results for primary repair. The trend is quite apparent and the weight of evidence is in favour of primary definitive repair, even in the youngest infant.

By accident of time, the chapter that deals with prosthetic valves is out of date and incomplete in that it does not include reference to the Björk-Shiley and Lillehei-Kaster valves. None the less, it contains a great deal of original material on thromboembolism related to prosthetic heart valves and is worth while reading.

Another chapter details much of the recent work on myocardial flow and on subendocardial ischemia during cardiopulmonary bypass. Every surgeon engaged in cardiac surgery should be thoroughly familiar with the contents of this chapter.

A high standard of excellence is maintained throughout the book, although the author of the discussion on reconstructive surgery in coronary artery disease does not appear to have entirely crystallized the surgical indications.

The few mistakes are typographical; they do not change the meaning of the text and will, no doubt, be corrected in future editions.

This important book deserves a place on the library shelves of every clinician dealing with diseases of the heart—congenital or acquired.

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ATLAS OF ORTHOPAEDIC SURGERY. 2 vols. Louis A. Goldstein and Robert C. Dickerson. 1039 pp. and index. Illust. The C. V. Mosby Company, St. Louis, 1974. $91.90.

This book cannot be lightly reviewed. It is a major, profusely illustrated publication in two volumes, and the first edition of such a work presented for students and orthopedic surgeons. The illustrator, Walinitz, deserves recognition for his 1674 illustrations, and perhaps his name should figure on the cover. At the price of $91.90 this beautifully produced and bound work must be one of the most expensive medical textbooks on the market. Actually, I am not prepared to complain of such a price for a tool of the trade; compare it with that charged for some small, simple, orthopedic instrument.

Is there a need for such an extensive atlas of orthopedic techniques? On consideration, there is indeed. How do we learn the steps of a procedure? How do we recall an unusual technique or the stages of an intricate operation? Possibly by repetition, or by example, but often by reference to a standard text, a monograph, a journal or by a chat with a colleague. Unless we are engaged in a high-volume practice, repetition alone is not reliable so we depend on the other means. This atlas of Goldstein and Dickerson (and Walinitz) describes well the stages of most standard procedures but fails to list the advantages and disadvantages of others. Actually, a quick reference to an author's original description of his procedure is a most valuable preparation for embarking on many a procedure; one is often surprised at the inaccuracies that have crept into the collected texts. I find myself referring more regularly to the original monograph on many an operation. Unfortunately, it is often hard to lay hands on the right reference at the right time.

The two volumes are divided into a total of 16 sections on various anatomical regions. There is a rather loose section entitled "Miscellaneous Operative Procedures" which includes advice about repairing tendons, arteries, arthroscopy, release of contractures, and even localization of metallic foreign bodies.

One misses any reference to incisions and approaches. Within the sections there is usually a quite lengthy description of postoperative care, often repeated. Thus, the description of each form of ankle fusion is followed by a note that a cast is required and may be removed when there is radiographic and clinical evidence of fusion—surely such details could be generalized in a preamble.

The scope of techniques described is extensive; I have no quarrel with the authors' (and Walinitz's) choice. However, it may be unnecessary to devote so much pictorial art to

say, "disarticulation of the wrist" (surely a rare operation) and the "internal fixation of a fractured clavicle".

In each section the text (including generalizations) and description appear on the page opposite to the handsome illustrations. This means that, in many cases, an almost blank page is found facing the reader, which perhaps explains the need for two volumes. There are extensive references but no mention is made to them in the text and this is irritating; for example, if I wanted to look up references to Dupuytren's contracture I would have to search the alphabetical list of authors in this section on the hand to ferret out the original description of the condition—a most confusing arrangement.

This work will probably become established as a standard reference for orthopedic libraries, to whom I would recommend it. There certainly seems to be a need for collected descriptions of this sort.

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CLINICAL NEUROSURGERY. Proceedings of the Congress of Neurological Surgeons, Honolulu, Hawaii, 1973. Editor-in-Chief: Robert H. Wilkins. 387 pp. Illust. The Williams & Wilkins Company, Baltimore; Burns & MacEachern Limited, Toronto, 1974. $21.45.

This excellent book comprising the papers and discussions presented at the 1973 annual meeting of the Congress of Neurological Surgeons, provides the most up-to-date authoritative work on the subjects presented. The book is published once a year following each meeting, and for every practising neurosurgeon, and to a lesser extent neurologists, neurophysiologists, and vascular surgeons, it is well worth the price. No one volume covers the entire field of neurological surgery but each volume covers all significant current developments, new techniques, and discussions of controversial problems on the topics selected for that year. In this particular volume, 11 of the 29 chapters are devoted to saccular aneurysms and the various forms of management, 10 chapters to pain, 5 chapters to pituitary surgery and related conditions, and 2 to malignant tumours.

With the passage of time, each volume of "Clinical Neurosurgery" becomes more valuable, not only for the information it contains but as a library possession since it is printed in limited editions. This volume is a concise, up-to-date, well-printed ready reference. The publication is unsurpassed in its field.

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SURGICAL PATHOLOGY. 5th ed. Lauren V. Ackerman and Juan Rosai. 1394 pp. Illust. The C. V. Mosby Company, St. Louis; The C. V. Mosby Company, Toronto, 1974. $47.80.

The fifth edition of "Surgical Pathology" continues in the tradition of previous editions with emphasis on the most practical aspects of pathology as it pertains to surgery. The references have been updated and over 300 new illustrations added. Sections on exfoliative cytology have been added where applicable. Mention is also made of electron microscopy, immunofluorescence and histochemistry where particularly relevant. The book is full of well-selected pictures illustrating the gross and microscopic features of all the common and many of the less common diseases encountered in general surgery and in specialty surgical practice. The book is not exhaustive and is not intended as a theoretical text. For instance, discussion of theories of etiology and pathogenesis of diseases are not included. The main thrust of the text is clinical-pathological correlation and prognosis. Most tumours are well discussed and the chapters on diseases of the skin, breast, gastrointestinal and respiratory tracts and on gynecopathology are particularly well done.

This is an extremely useful book for pathologists and surgeons. I strongly recommend it to both.

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SYMPOSIUM ON AESTHETIC SURGERY OF THE NOSE, EARS, AND CHIN. Volume Six. Edited by Frank W. Masters and John R. Lewis. 207 pp. Illust. The C. V. Mosby Company, St. Louis; The C. V. Mosby Company Ltd., Toronto, 1973. $39.40.

This book comprises the papers that were presented at a limited symopsium organized by the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons on plastic surgery of the nose, ears and chin.

Almost two-thirds of the book is devoted to the nose. An account of historical aspects is followed by a discussion of anatomy and physiology. Standard techniques for aesthetic rhinoplasty are described, including comparison of saw with osteotome techniques and management of the nasal tip. There are good sections on the cause, prevention and management of complications. There are papers devoted to septoplasty and to the management of acute and late problems from nasal trauma. There is minimal coverage of reconstructive

procedures after cancer excision, the use of cryosurgery for malignant tumours and the treatment of rhinophyma, for which only one method is mentioned.

The papers devoted to the ears merely present a confusing array of different methods of set-back otoplasty without useful comparisons. The problems of cryptotia, microtia and the "lop-ear" are barely covered.

The final chapters on the chin simply discuss silicone implants in microgenia. There is no discussion of sliding genioplasty or the relationship between microgenia, micrognathia or retrognathia.

This book merits inclusion in the plastic surgery section of a hospital library but is of little use to the surgeon trying to learn techniques or attempting to decide which technique is best.

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UROLOGY. A View Through the Retrospectroscope. John R. Herman. 182 pp. Illust. Harper & Row, Publishers, Inc., Hagerstown, Md., 1973. $7.95.

In his preface, the author states that this book "should not be expected to serve either as a reference source or as a handbook for researchers in the field. If this work comes into the hands of medical students or residents and inculcates a sense of enjoyment of medical history, it will have served its purpose." In compliance with these introductory remarks, the author seems to have achieved his purpose.

This is a small book of 16 short chapters. It opens with an account of ancient and medieval urology from the eras of Egyptian papyri and indu Vedas and Samhitas. Understandably, prominence is given to urinary calculus because of its long and colourful history. Catheterization is traced from the earliest primitive methods to modern times. Reference is made to three important events in renal surgery: Vesalius (1514-1564) contributed to the understanding of human renal anatomy; Domenic Marchetti in 1680 performed the first nephrolithotomy; and Gustav Simon in 1869 successfully carried out the first planned nephrectomy. The chapter on the development of the cystoscope gives a consecutive account of the various inventions that ultimately led to the modern instrument. The author aptly refers to the new diagnostic horizon introduced by the discovery of x-rays, and to the men who participated in urological advances resulting from this invention. On the subject of the prostate gland, he begins with Herophilus of Chalcedon about 300 BC and concludes with the advent of transurethral resection—certainly not a thorough account but enough to give an idea of the progress of events. Bladder tumours are surveyed from the first monograph on the subject, published by Lacuna in Rome in 1551, to the important work of Edwin Beer and others in the early 20th century. Urinalysis is traced from the earliest period when uroscopy defined a multitude of pathological observations. Other areas of discussion are syphilis and gonorrhea, urethral stricture, aphrodisiacs, and dead-ends in urology. The last-mentioned form an interesting chapter on odd urological procedures that have become obsolete.

There is no bibliography, but a list of titles of books for recommended reading is included. While a number of important subjects have been omitted, this is in keeping with a small book which, in the author's words, "aims only to impart some of the fascinating background of the oldest of surgical specialties". The book is limited in scope but easy to read, and should constitute a welcome addition to a doctor's bookshelves.

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THE YEAR BOOK OF SURGERY 1973. Edited by Seymour I. Schwartz. 479 pp. Illust. Year Book Medical Publishers, Inc., 1973. $15.00.

The annual "Year Book of Surgery" is always a welcome arrival. The book consists of short summaries of articles that were published during the preceding year and that the editors regard as being of significant interest. Each article is followed by concise and critical editorial comment, which helps to put it in perspective. This year's edition follows the well-trodden path of previous success. The book is probably of major interest to the general surgeon, although articles on such general topics as food and electrolytes, wound healing, infections, burns, trauma, and shock may appeal to all surgeons. Orthopedics is not covered. Individuals with a research or clinical interest in a small area will find the coverage of that area somewhat meagre. The book, however, does cover most areas of immediate general clinical application. The "Year Book of Surgery" provides the busy surgeon with an excellent means of keeping up-to-date.

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INDEX TO ADVERTISERS

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Acute Fluid Replacement in the Therapy of Shock. Edited by Theodore I. Malinin, Robert Zeppa, William R. Drucker and Arthur B. Callahan. 307 pp. Illust. Stratton Intercontinental Medical Book Corporation, New York; Longman Canada imited, Toronto, 1974. $27.00.

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